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cancer registry a pacemaker

The American College of Surgeons recently announced an addition to the categories of cancer facilities for which it formulates standards and that are eligible for its approval. On January 1, 1955, the Hospital Cancer Registry will join the cancer services that at present include the familiar cancer hospitals, cancer diagnostic clinics, and cancer clinics. For many years, the College has endeavored to improve the quality of cancer treatment, and the new Hospital Cancer Registry has that objective.

It is likely that most of the cancer in this broad country is not treated in the great medical centers by specialists who see large numbers of patients with cancer but, rather, in the hospitals of less than 200 beds, which account for some 86 per cent of all the approved hospitals in the country. What happens to this large volume of cancer is unknown. Dispersed as it is among so many hospitals, few surgeons and radiotherapists see enough of it to justify reporting their end results. Yet in the aggregate, the cancer experience of the smaller hospitals represents the greater part of the total cancer picture, and therefore it influences the national cancer mortality more importantly than does the experience of the university hospitals and medical centers.

The Hospital Cancer Registry as now recommended by the American College of Surgeons will, if widely adopted, provide the means of determining and evaluating the quality of the treatment on which most cancer patients depend.

It is of interest, and somewhat humbling, to note that this enterprise was urged as long as twenty-five years ago. In 1928, the American Society for the Control of Cancer (now the American Cancer Society) requested Dr. H. C. Saltztein to undertake a survey of facilities for care of cancer patients available in the average American city. His report of that survey was published in the J.A.M.A. for August 18, 1928, and among the conclusions was this:

"The records of cancer cases could be pooled through individual hospital follow-up reports, or through a central bureau embracing the hospitals of a city. This is not hard to start, and on the whole is not expensive."

And even before that, indeed fifty years ago, Thomas S. Cullen,* the Johns Hopkins gynecologist, was writing "This is an age of time-saving devices and all business men are keen to see what results have accrued from their endeavours. What applies to business applies equally well to the subject of cancer. What is the use of operating year after year in a routine manner, having but a hazy idea of what has finally become of the patient. At least one tactful clerk in every hospital should be assigned to the task of keeping in constant contact with those who have been operated on. In this manner one can at a glance tell how many patients have been relieved . . . The results of one operator are compared with those of another—of course in a most friendly way, and there is no doubt that a runner can always make better progress with a pacemaker."

We hail the College's proposal of the Cancer Registry as the long-awaited pacemaker!

*Cullen, T. S.: Address in gynaecology. Canad. M. A. J. 3:658-671, Aug., 1913.

Cover—
"Muscleman" of Vesalius. From: De Humani Corporis Fabrica, Padua, 1543.

NEWSLETTER

JANUARY, 1954

(Continued from CA 3: November, 1953.

University of Southern California: Jones and Macdonald reported that a significant percentage of cervical-cancer patients have a common background of these factors: marriage before age 18, completion of childbearing before 25, low economic status, and divorce, separation, or widowhood. Rittenberg has found evidence that about 30 per cent of the energy in food is retained by the body as a sort of fuel that can be used to spark metabolic processes. Kotin and others are raising mice in a chamber filled with synthetic "smog" to determine whether polluted atmosphere is carcinogenic. Field described the growing U.S.C. drug-screening program and mentioned good palliative effects achieved with TEPA against melanoma and with 6-mercaptopurine against some leukemias. Visser outlined a program that is mass-producing nucleoside analogues, which are being tested elsewhere against cancers and viruses. Zinsser has been inserting a radiotransmitting probe into the bladder and determining by the wave-reception patterns the status of bladder tumors. Field and Starr are investigating possible relationships between radioactive-iodine thyroid therapy and cancer.

Cal. Tech: Borsook and others now have found three groups of substances that accelerate protein synthesis and one group that inhibits it. When all the substances are analyzed and their mechanism of action determined, man will understand and be able to exercise new control on some diseases -- possibly cancer. Galston outlined the influence of auxin on the growth and aging of plants, auxin's inactivation by enzymes, and the braking action of catalase on the inactivating enzymes. Bonner's work -- a new concept of how a hormone (indole acetic acid, in this case) chemically controls growth -- was described.

Cedars of Lebanon Hospital: Henstell charted the influence of DNase and its inhibitor on the growth and maturity of cells. He asserted that the immaturity and lawlessness of leukemic cells seems due to their lack of inhibitor.

M. D. Anderson Hospital: The impressive new -- as yet uncompleted -- building and its ultramodern radiation facilities were shown. Macdonald declared herself still unconvinced (on the basis of statistical evidence so far produced) of the relationship between cigarettes and lung cancer. Wynne and others have found that a battery of twenty-five bacteria, each batch maintained on diets deficient in a single nutrient plus patient's blood, are showing differences in cancer and normal blood -- better than any "blood test" thus far investigated. Trunnell and others have launched a gigantic metabolic study covering such points as: (1) characterization of a blood factor (found most often in menstruating women) that destroys animal cancers in culture, (2) tracing the steroid hormones' chemistry in normal and cancer tissues, (3) enzyme relationships to hormones, and (4) the morphogenetic development of thyroid cancers. Cobb asserted that people in the higher social, economic, and intellectual brackets (and particularly women) were most prompt in calling cancer symptoms to the doctor's attention. She indicted cancer-education authorities for failing to reach the less literate millions with life-saving messages on symptoms. Wheeler now is giving psychological and personality tests to patients with hormone-dependent cancers to determine whether there is any correlation between personality factors and response to hormone therapy. Wingo told of efforts to measure growth (in these experiments, of Tetrahymena) and to establish precise standards for determining the efficiency of growth inhibitors and stimulants. Jirgensons described the development of new chemical and physical methods of characterizing pure proteins from blood and urine (particularly their colloid-chemical properties), which eventually might lead to earlier and more accurate cancer diagnosis.

University of Texas: Pomerat and Hsu at the University of Texas in Galveston related the story of a happy accident (in which cultures were bathed in a hypotonic rather than isotonic solution) resulting in the dramatic spreading of chromosomes so they could be counted under the microscope. Cancer cells show a remarkably high number of chromosomes and shattered chromosome fragments.

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Keeping up

Urology and Cancer Prevention

The author reports a series of studies designed to throw further light on the available methods in the prevention and treatment of cancer of the genitourinary system and suggests several procedures that may effectively reduce the frequency of this condition. First recognized by Rehn and later proved by Hueper is the factor of preventable occurrence of bladder cancer in aniline dye workers. β-naphthylamine has been isolated as the principal carcinogenic agent in these patients. To prevent benign papillomas of the bladder from developing, almost invariably, into bladder cancer, these lesions should be excised or fulgurated. The greater frequency of penile cancer occurring in patients not circumcised or circumcised in adult life as opposed to the almost nonexistent occurrence in men circumcised in infancy is also summarized. Another condition that contributes to the preventable occurrence of prostatic cancer is discussed: The administration of testosterone or other androgenic steroids to men more than 50 years old is discouraged because of the delicate estrogen-androgen equilibrium associated with prostatic cancer and the likelihood of activating clinically quiescent carcinoma of the prostate. Quantities of estrogen as small as 0.25 mg. of stilbestrol daily, administered intramuscularly, will produce remission of advanced prostatic cancer. This beneficial effect is completely neutralized by the simultaneous daily administration of 10 mg. of testosterone propionate.

Baker, R.: Studies on cancer prevention in urology. I. Prostate. Ann. Surg. 137: 29-35, Jan., 1953.

An International Uterine-Cancer Study

An international investigation of the racial and geographical distribution of cancer of the uterine cervix, initiated in September, 1951, offers an interesting field for the study of the possible etiological factors in this disease. Observations encompassing a wide range of ethnic and religious groups point to possible differences in racial and religious customs and hygienic conditions that may contribute to increased or decreased occurrence. In the United States, the frequency of cancer of the uterus in the Negro population is 60 per cent higher than that in the white population. A clue to preventive measures in respect to cervical cancer may be found in the study of the lowered racial incidence in Jewish women. Clinical studies now being conducted in two areas —New York and Israel—are designed to acquire the basic information necessary to compute the incidence rates for cancer of the uterine cervix and the fundus in Jewish and non-Jewish women.

Symeonidis, A.: An international uterine cancer study. New York Med. 9:160, Feb. 20, 1953.

The G. P. and Gynecological Cancer

Generally, gynecological cancers are favorably situated and the diagnostic procedures involved are not complex or expensive. Cancer-detection clinics and the routine screening of gynecological patients by means of the vaginal smear have shown that it is possible to diagnose cancer of the cervix when the cervix is almost normal in appearance or the site of an apparently benign inflamed erosion. The use

with Cancer

of a bivalve speculum in a good light will uncover many lesions that would remain unrecognized if one depended entirely on the examining fingers. In recent years cancer of the body of the uterus has been found to be relatively more common than previously believed. Abnormal bleeding in the premenopausal period and recurrence of bleeding after the menopause suggest the possibility of corpus cancer. Fibroids, nulliparity, and a delayed menopause are all associated with corpus cancer. In cancer of the ovary, early pain is often due to digestive distress from secondary peritoneal implantation, and, in women older than 40, complaints of indigestion should lead to pelvic examination. Estrin used to control disturbances of the menopause is often responsible for a diagnostic problem. Although it is doubtful that it has ever caused cancer in women, endometrial overgrowth and hyperplasia may be extreme and the associated bleeding alarming. Curettage alone answers the question. The sympathetic interest and guidance that the family physician can give to the chronically ill patient should not be dismissed merely as the terminal care of the cancer patient. It epitomizes the practice of a good physician.

Cosbie, W. G.: Gynaecological cancer as seen by the family physician. In *Anon.: Annual Report; Ontario Cancer Treatment and Research Foundation. Toronto, Canada. 1951; pp. 16-20.*

Use of Vaginal-Smear Technique in Mass Cancer Screening Project

A preliminary analysis of 20,000 women studied by the vaginal-smear technique in a mass-screening cancer survey is discussed. Follow-up data on this investigation initiated toward the end of 1952 are necessarily incomplete. In the first 10,000 women, 90 per cent of the smears were negative, 6 per cent unsatisfactory, and in 4 per cent either additional smear examination or biopsy was requested. Biopsy examination was requested on 181 positive or suspicious cases (1.8 per cent of the total). The biopsy on 150 of these has been examined and about 50 per cent (seventy-three cases) proved to be either intraepithelial or invasive cancer. At least thirty women whose clinical histories or findings were noncontributory would not have been diagnosed at that time except by the use of the exfoliative cytology method. Results of the second 10,000 women examined indicate similar findings, i.e., biopsy was requested on about 1.8 per cent and so far about 50 per cent of the biopsies have provided confirmation of invasive or intraepithelial carcinoma.

Erickson, C. C.; Everett, B. E., Jr.; Siegler, E. E.; Whitacre, F.; Stirling, J.; Dunn, J. E., Jr.; Graves, L. M., and Sprunt, D. H.: Preliminary report of 20,000 women studied by the vaginal smear technic in a general population cancer screening project. [Abstr.] Proc. Am. A. Cancer Research 1: 14-15, April, 1953.

Current Cancer Chemotherapy

A review of the current chemotherapy of cancer is presented with emphasis on the limited range of efficacy of available drugs. Substances are classified according to their mode of action into three groups: those producing an unfavorable environment for the cancer cell, those modifying the systemic intoxication produced by cancer, and those that damage the cellular functions. Although significant contributions have been made by chemical compounds employed as palliative agents

in patients with metastases, with the exception of the hormones the chemical compounds used in destroying neoplastic cells would be lethal to normal cells as well, thus precluding curative therapy. Another limitation is the small number of tumor types that respond to drugs. The malignant lymphomas and leukemias, which constitute a small fraction of all malignant neoplastic diseases, have been treated with urethane, folic acid antagonists, cortisone, and the nitrogen mustards. The empirical approach has largely consisted of screening chemical compounds for their effect on the growth of transplantable tumors in mice, rats, and rabbits. With the possible exception of mouse leukemia, there is no evidence to demonstrate that transplantable or spontaneous tumors in laboratory animals are biologically directly comparable to human tumors. One apparent discrepancy between experimental and human tumors is in their relative growth rates. The cells of experimental tumors divide rapidly, whereas human epithelial tumors grow relatively slowly. It may be significant that the drugs that are active in the currently employed animal-tumor screening tests are effective principally against the most rapidly growing human tumors. The question is whether screening techniques are missing potentially useful compounds against other tumors. The author suggests that more subtle end points than the ones now in use might indicate chemical compounds that fail to produce dramatic changes in tumor growth after brief administration but that might modify the growth of tumors when given over long periods.

Gellhorn, A.: A critical evaluation of the current status of clinical cancer chemotherapy. Cancer Research 13:205-215, March, 1953.

Management of Pain of Cancer

Many of the 200,000 persons who die each year from cancer in the United States suffer severe pain during their last months of life. The pain becomes progressively more severe and finally develops into a relentlessly agonizing suffering that all too soon causes physiological as well as psychological deterioration. The deplorable attitude of defeatism found in some quarters must be replaced by courageous aggressiveness tempered by sound judgment. The following factors are responsible for the pain: compression of nerve roots, trunks, or plexuses by the tumor or by pathological fractures of bones adjacent to the nerves; infiltration of nerves and blood vessels by tumor cells, resulting in perivascular or perineural lymphangitis and irritation of sensory nerve endings, and producing a diffuse burning pain, the so-called sympathetic pain; obstruction of a viscus, with production of true visceral pain; occlusion of blood vessels by the tumor; infiltration, tumefaction, and swelling in tissue invested snugly by fascia, periosteum, or other pain-sensitive structures; necrosis, infection, and inflammation of pain-sensitive structures causing pain that is sometimes excruciating. The author briefly comments on the importance of psychological support for these patients and on palliative operation but is concerned chiefly with nerve blocking. Analgesic block, when properly executed and effective, affords adequate relief without adding to the patient's discomfort. For pain of the face, mouth, tongue, throat, and neck, alcohol injection of the trigeminal nerve or its branches, the glossopharyngeal and vagus nerves, and/or the upper cervical spinal nerves is usually very effective. Pain below the neck can be controlled for weeks or months with subarachnoid alcohol block, paravertebral block, or injections of peripheral or intercostal nerves. Since in many of these cases the sympathetic nervous system is involved in the pain mechanism, sympathetic nerve blocks are occasionally necessary to alleviate the pain completely.

Bonica, J. J.: The management of pain of cancer. J. Michigan M. Soc. 52:284-290, March, 1953.

Carcinoma of the Cervical Stump

The incidence of carcinoma in the retained cervical stump, its mode of lymphatic spread, its best clinical evaluation, and its therapy are reviewed. Cancer of the cervical stump occurred in 4.1 per

cent of several series totaling 12,861 cases. Lymphatic spread from carcinoma of the cervical stump follows a constant pattern. This type of cancer may also spread by continuity, contiguity, and the blood vascular systems. Cases showing ureteral obstruction have a poor prognosis. Factors favoring surgery over radiation in selected stage-I and early stage-II cancers of the cervical stump include prediction of radiation-resistant cases, shortcomings of irradiation in the cure of involved regional nodes, local recurrence following apparently adequate radiation, technical difficulties of radium application to stumps bearing cancer, occasional stenosis of upper vagina following external roentgen-ray therapy, greater frequency of postradiation complications, and the success of surgery. Total hysterectomy is preferred whenever hysterectomy is indicated. It is important that every patient with a retained cervix be thoroughly instructed as to the need of periodic follow-up examinations. Surgery as an adjunct to irradiation therapy should be allowed broader consideration in cancer of the retained cervical stump than in carcinoma of the cervix.

Young, H. A., and Jonas, A. F.: Combined surgery and irradiation in the treatment of cancer of the cervical stump. Surg., Gynec. & Obst. 96:288-294, March, 1953.

Cytological Diagnosis of Cancer

An abrasive-balloon technique for obtaining cytological material from the stomach is described as a reliable diagnostic aid. Simple gastric aspiration and a variety of methods of lavage failed to produce material satisfactory for cytological interpretation. Two hundred and thirty-eight patients with gastric diagnostic problems were studied by this technique. Fifty-one patients proved to have malignant lesions of the upper gastrointestinal tract at operation, and positive smears were obtained in forty-five of these. The six false-negative cases occurred in patients in whom the physical characteristics of the neoplasm seemed to preclude the possibility that viable tumor cells would reach the surface of the gastric lumen. One definitely false-positive smear was reported among 187 patients shown to have nonmalignant conditions. Seven suspicious smears were reported in this group, yielding an over-all accuracy of 95.7 per cent for the negative-smear group. It is emphasized that although the balloon technique may be more accurate than roentgen rays in the detection of early lesions, it supplies no information as to the location or extent of the tumor. Rapid processing of the material obtained with the balloon, intelligent handling of the various fractions obtained by aspiration and rinsing of the balloon, and proper preparation of the stomach are important for success. Above all, a trained cytologist must be available to interpret the smears.

Cooper, W. A., and Papanicolaou, G. N.: Balloon technique in the cytological diagnosis of gastric cancer. J.A.M.A. 151:10-14, Jan. 3, 1953.

Thyroid Carcinoma—I^{131} Therapy

Since the first patient with carcinoma of the thyroid was treated with radioactive iodine ten years ago, more than 250 thyroid-carcinoma patients have been treated with I^{131}. Radioactive iodine is not indicated unless the patient has first had a total surgical thyroidectomy in order to prevent death from local growth of the primary tumor and to encourage the pituitary to stimulate metastases to a greater affinity for I^{131}. Roentgen-ray therapy should also be tried first as an adjunct to surgery before I^{131} is tried.

How can one tell in advance whether there will be a good response to treatment with I^{131}? Follicular and alveolar carcinomas most commonly show good response, papillary carcinomas less commonly. Undifferentiated carcinoma of the thyroid is a contraindication to I^{131} therapy. The four methods commonly used to test the ability of the cancer to concentrate I^{131} are described: autoradiography, external gamma counting, urinary excretion of I^{131}, and I^{131} level in the circulating blood. A more nearly complete response can be promoted by increasing the thyroid-stimulating–hormone (TSH) effect on metastases through total thyroidectomy, thiouracil administration, and ex-

ogenous administration of TSH. Three temporary contraindications to I^{131} therapy include clinical myxedema, administration of desiccated thyroid or iodides, and the presence of hypoplasia of bone marrow.

Beierwaltes, W. H.: Indications and contraindications for treatment of thyroid cancer with radioactive iodine. Ann. Int. Med. 37:23-30, July, 1952.

Papilloma of the Gallbladder with in Situ Carcinoma

True papilloma of the gallbladder is rare. The authors estimate its incidence about 1 in 100 cholecystectomies. It is sometimes confused with cholesterol polyps or with the epithelial proliferations seen in chronic cholecystitis. The diagnosis of true papilloma of the gallbladder requires cholecystography. Four patients with papilloma of the gallbladder who were recently observed at Memorial Hospital in New York City are described. These cases were considered especially noteworthy because noninfiltrating carcinoma in situ originated in the papilloma in three of the patients. Cholecystectomy is the recommended treatment of papillomas of the gallbladder, because this condition is capable of giving rise to symptoms, because it is frequently associated with cholecystitis and cholelithiasis, and, most important, because it is a precancerous lesion highly capable of becoming malignant.

Tabah, E. J., and McNeer, G.: Papilloma of the gall bladder with in situ carcinoma. Surgery 34:57-71, July, 1953.

Total Prostatectomy in Carcinoma of Prostate

Castration and the estrogens have had a profound effect upon cancer of the prostate but there is little evidence that these measures are curative. One hundred total prostatectomies performed at the Massachusetts General Hospital during the past twenty years for suspected cancer were reviewed. In spite of clinical evidence that cancer was present, no malignant disease existed in twenty-one. It should be recognized that early cancer of the prostate produces no symptoms. Symptoms present when the cancer is in an early stage usually are due to associated benign hypertrophy. Perineal biopsy and examination of frozen sections proved the most reliable diagnostic procedure. Of the forty-one patients who underwent total prostatectomy before 1949, twenty-six or nearly two thirds were clinically free of disease at the end of three years. Fifteen of the twenty-nine patients were alive and clinically free of disease five years after total prostatectomy. Ten had died of cancer. Total prostatectomy is gaining in favor to the extent that nearly four times as many of these operations have been performed at the author's clinic during the past ten years as during the previous decade. It is felt that functional results are sufficiently good to justify the procedure.

Colby, F. H.: Carcinoma of the prostate: results of total prostatectomy. J. Urol. 69:797-806, June, 1953.

Histological Grading of Cancer of Uterine Cervix

A survey of the various methods of histological grading of cervical carcinoma is evaluated. Schottlaender and Kermauner in 1912 suggested the system that has since become standard in many European countries. The tumors are first divided into adenomatous and solid types. The solid carcinomas are graded as mature, semimature, and immature. Broders of the Mayo Clinic in 1920 and 1922 developed a method that divides the tumor into differentiated and undifferentiated parts, and then, according to the relative amounts of the two types, it is assigned one of four grades. This method is the one most frequently used in North America. Other methods have been introduced but all these methods of histological grading are based on the degree of anaplasia versus differentiation. There is a poor correlation between the degree of anaplasia and the clinical extent of disease when the patient is first seen but somewhat better with the incidence of metastases in postmortem material. Radiotherapy results in a moderately higher "cure" rate in differentiated

tumors than in anaplastic ones. Some results of surgically treated highly anaplastic tumors are poor. It is concluded that histological grading is of limited prognostic value in cancer of the cervix.

Graham, J. B.: Histologic grading of cancer of the uterine cervix. Surg., Gynec. & Obst. 96:331-337, March, 1953.

Irradiation Treatment of Cancer Coexisting with Pregnancy

Two pregnant women with Hodgkin's disease and three pregnant women with cancer of the breast, lymphosarcoma, and leukemia respectively were given roentgen-ray treatment. With the exception of the woman with leukemia, the patients were delivered of normal babies. The spleen area in the leukemic patient was irradiated, suggesting the advisability of terminating the pregnancy. Twin fetuses removed by hysterotomy showed no ill effects of irradiation. The patient died shortly after the operation. The patient with cancer of the breast had an apparent arrest of the malignant process for a time after the delivery. Her condition gradually deteriorated and she died. The patient with lymphosarcoma, whose lesions remained quiescent during pregnancy, manifested symptoms with enlargement of the lymph nodes in the neck after the delivery of her baby. Roentgen-ray treatment was repeated and she improved again. The two women with Hodgkin's disease are in good condition, and the children are normal and healthy. A sixth patient, a 42-year-old pregnant woman with cancer of the tongue, was given treatment with the 5-gm. radium pack through the right mandibular, right submental, and left mandibular areas. A total of 37,500 mg.-hr. was given to each area. There was a fair response to treatment, and the patient was delivered of a normal full-term infant. The procedure to follow in a woman with a malignant lesion who is also pregnant depends on the extent and character of the malignant lesion and the stage of the pregnancy. Because of the known stimulative effect of pregnancy on malignant tissues, women who have a malignant condition should not become pregnant and should be sterilized to prevent pregnancy. Irradiation over the unborn fetus at an early stage necessitates immediate therapeutic abortion. Direct irradiation of the pregnant uterus should be avoided. When this precaution is followed children born of irradiated mothers are normal in every way.

Kaplan, I. I.: Successful irradiation treatment of malignancy coexisting with pregnancy. New York State J. Med. 53:1215-1218, May 15, 1953.

Pancreaticoduodenal Cancer

The results of radical resection of pancreaticoduodenal carcinoma, which includes tumors of the head of the pancreas, the ampulla of Vater, the common bile duct, and the duodenum, are presented. The results of both curative and palliative surgical treatment in the 183 patients treated during the last decade (1941 to 1950) are compared with the clinical course of the same types of carcinoma in 132 patients treated during the preceding decade (1931 to 1940). In the earlier decade only palliative surgery was employed regardless of the size of the tumor, duration of symptoms, or condition of the patient. The conclusion drawn from the comparison of these two groups is that little or nothing has been accomplished by pancreaticoduodenectomy if the results are viewed from the standpoint of overall salvage. In some cases radical resection has been of palliative value and, in a still smaller group, has achieved five-year survival and possibly permanent eradication of the disease. The authors feel that recently described methods of resection of the portal vein and accompanying lymphatics may improve the results obtained by the radical surgical removal of these tumors.

McDermott, W. V., Jr., and Bartlett, M. K.: Pancreaticoduodenal cancer. New England J. Med. 248: 927-931, May 28, 1953.

at a glance . . .

one-minute abstracts of the current literature on cancer . . .

Bone Cancer—Diagnosis

Early correct diagnosis of bone cancer is essential in order to ensure prompt and proper treatment. Following a careful history and complete physical examination, the patient should be referred to the roentgenologist. Blood studies should then be made. Clinical, roentgenographic, and chemical findings should then be corroborated by microscopic study of biopsy material. If a bone lesion or disease process has been proved to be present, it must be decided whether the lesion is a tumor and, if it is a tumor, whether it is benign or malignant. An outline of a complete diagnostic work-up is presented. The physician should be suspicious of the presence of bone cancer in any patient with pain, swelling, and disability not obviously explainable on other grounds.

The following are malignant tumors of the bone: osteogenic sarcoma (fibrosarcoma and chondrosarcoma), Ewing's sarcoma (endothelioma), reticulum-cell sarcoma, malignant giant-cell tumor, angiosarcoma of bone, myeloma, and metastatic cancer (breast, prostate, kidney, thyroid, lung).

Coley, B. L.: Diagnosis of cancer of the bone. New York State J. Med. 52:2984-2988, Dec. 15, 1952.

Chondrosarcoma of Bone

Chondrosarcomas are relatively rare, only 7.6 per cent of the primary malignant bone tumors entered by the Registry of Bone Sarcoma of the American College of Surgeons being chondrosarcomas. Fairly reliable prognostic evaluation is possible by pathological study of the chondrosarcomas. They may be graded according to the relative incidence of atypical nuclei. Cartilaginous tumors of ribs, sternum, vertebrae, pelvis, clavicle, and scapula are either actually or potentially malignant in a high percentage of cases. It is possible that all enchondromas that do not become quiescent after adolescence develop into overt chondrosarcomas. Large enchondromas that have greatly expanded the cortex and especially those that have perforated the cortex in the absence of trauma should be considered as probably malignant. Multiple cartilaginous exostoses that continue to grow, especially if they grow at an increased rate or first appear after the age of 22, should be considered malignant.

If a diagnosis of equivocal or low-grade chondrosarcoma can be made by clinical and radiographic methods, it would seem best not to make a biopsy. Biopsy is, of

course, expeditious and safe in accessible sites, in cases in which amputation is planned, or in those in which the biopsy wound can be excised during radical resection if the tumor proves to be malignant. Biopsy has the disadvantage that it may spread tumor cells.

Amputation is the treatment of choice in chondrosarcoma and should preferably be proximal to the bone of origin. While local resection is feasible in some selected, untreated, low-grade chondrosarcomas, it is not often successful in treatment of recurrent chondrosarcomas. Roentgen-ray therapy is not recommended in the primary treatment of chondrosarcoma and generally has little success when administered for palliation.

O'Neal, L. W., and Ackerman, L. V.: Chondrosarcoma of bone. Cancer 5:551-577, May, 1952.

Ewing's Sarcoma

An analysis of a group of fifty cases of Ewing's sarcoma treated at the Massachusetts General Hospital indicates that results of treatment are likely to be better with roentgen-ray therapy than with attempts at surgical eradication. Seven patients survived for more than five years—six after radiation therapy, and one after radical surgery. Five of these patients were apparently cured; two ultimately died of the disease. The experience of these authors confirmed previous impressions about Ewing's sarcoma. It is a highly malignant, radiosensitive neoplasm that usually involves bones in a location below the waist. The majority of patients are young people (in this series, two thirds were less than 20 years old). The malignancy of Ewing's sarcoma appears to vary considerably. In the present group of the twenty-two treated by radiation aimed at cure, fifteen were locally controlled, and of these four survived for more than five years without disease. Of fourteen patients who showed distant disease when first seen and whose treatment was palliative only, one lived for three and a half and one for seven years before succumbing to the disease. The radiographic appearance of the tumor may resemble osteogenic sarcoma closely and may simulate osteomyelitis in both its clinical and radiographic aspects.

Wang, C. C., and Schulz, M.D.: Ewing's sarcoma; a study of fifty cases treated at the Massachusetts General Hospital, 1930-1952 inclusive. New England J. Med. 248:571-576, April 2, 1953.

Diagnosis of Bone Tumors

Persistent bone, joint, or muscle pain, especially when the involved part is at rest, should suggest the possibility of a primary malignant tumor of bone, and further studies beginning with a roentgenogram of the affected area should be instituted. A correct diagnosis can be made in the majority of cases of primary malignant bone tumors on the basis of careful history, complete physical examination, essential laboratory studies, roentgenograms, and biopsy. Laboratory examination should include urinalysis, estimation of hemoglobin concentration, complete blood-cell and differential counts, Wassermann reaction, erythrocyte sedimentation rate, and serum-phosphatase level. Significant information is furnished by roentgenograms, not only of the bone or bones at the site of symptoms, but also of the lungs, if the initial film shows a bone lesion. Surgical biopsy of all patients is recommended to determine the type of treatment to be instituted, the needle-biopsy technique described by Rex and Brooks being performed most frequently. In addition to a report of grade of malignancy, the pathologist may provide valuable information in effecting a decision as to type of therapy.

Haggart, G. E., and Copel, J. W.: Early diagnosis of primary malignant bone tumors. J. A. M. A. 152: 883-885, July 4, 1953.

Fractures in Metastatic Carcinoma

The authors believe that a hopeless "do nothing" attitude is not justified in treating fractures from metastatic carcinoma. A vigorous plan of treatment, which often involves an open reduction and internal fixation, will frequently relieve pain, decrease the length of hospitalization, permit early ambulation, and make nursing care easier. Case reports are given to show that

intramedullary nailing is often ideal for the treatment of these injuries. Fifty patients with fractures caused by metastatic carcinoma are analyzed. Carcinoma of the breast accounted for half of the fractures. The spine, femur, and bones of the shoulder girdle were most frequently fractured. Twenty-two per cent of the fractures healed, although almost half of the patients died from progression of the disease within six months of fracture.

Fitts, W. T., Jr.; Roberts, B., and Ravdin, I. S.: Fractures in metastatic carcinoma. Am. J. Surg. 85: 282-287; disc. 287-289, March, 1953.

Soft-Part Tumors—Treatment

Lesions of the soft parts may be malignant and early diagnosis and prompt treatment may be essential if the life of the patient is to be saved. Many painless swellings of the soft parts may represent harmless conditions such as sebaceous cyst or lipoma, and the tendency is to assume at the outset that soft-part tumors are benign, whereas the writer thinks it a safer policy to assume that they are malignant until the entire tumor has been examined by a pathologist following a wide excision. When seen for the first time, a soft-part tumor should, if possible, always be widely excised and not merely cut into for biopsy purposes. More aggressive surgical extirpation at the beginning may, in the long run, prove to be conservative surgery and may be life-saving. After one well-conceived and -executed excision has failed, the next procedure to be considered is amputation if such is technically feasible.

Coley, B. L.: Treatment of soft part tumors. [Editorial.] Am. J. Surg. 84:259-260, Sept., 1952.

Radiation Effects upon Growing and Adult Bone

Formerly, adult bone was considered one of the most radioresistant of normal tissues. Now, soft-tissue components of the bone, such as the terminal blood vessels of the haversian and Volkmann's canals, are recognized as being particularly affected by hyperemia and later by obliterative endarteritis. With the present tendency toward the use of higher and higher voltages for therapy and with delivery of increasing amounts of radiation to the deeper tissues, it should be remembered that repetitive treatment tends to produce damage out of proportion to the amount given, probably because recuperative capacity is diminished by previous irradiation. Osteoporosis of the bone following irradiation may be the result of a disturbance in the normal balance between resorption and production of bone and, although it may look strong roentgenographically, any sudden or unusual stress or strain may produce a fracture. Fractures of the femoral neck should be suspected in all patients who complain of hip or thigh pain and difficulty in walking after heavy pelvic irradiation. Mention is made of a group of thirty-four children who had received radiation in which the spine was included. Exposures in excess of 2000 r to the spine invariably produced growth disturbances. The degree of disturbance appears to bear a definite relationship to dosage and reciprocal relation to age. The rate of delivery of the radiation and the over-all time are important factors in the production of injury.

Jacox, H. W.: Radiation effects on bone. [Editorial.] Radiology 59:744-746, Nov., 1952.

Adamantinoma of the Tibia

A 40-year-old Hindu "ward boy" was admitted to Gandhi Memorial Hospital, Lucknow, with a painful swelling on his left knee, extending from the tubercle of the tibia to about 3 in. about the patella. There was another small swelling about the middle of the left leg, fixed to the middle third of the fibula. Lymph nodes in the left inguinal region were enlarged. There was a history of injury to the left leg a year before. Histological examination of a specimen taken by punch biopsy from the tumor in the upper end of the tibia showed the structure of an epithelial tumor resembling an adamantinoma. Amputation was performed from the middle of the left thigh. On the basis of various sections taken from the tumor mass, the

punch biopsy, and the lymph-node biopsy, a diagnosis of primary epithelial tumor—adamantinoma of the tibia and fibula—with metastasis to the inguinal lymph nodes was made. The patient is now well except for enlarged nodes in the inguinal region for which he is being treated with deep roentgen rays. This is the thirteenth case of adamantinoma of the tibia to be reported in the literature. A history of trauma was available in almost all the cases. In the case under report, the tumor not only spread locally through the cruciate ligaments to the femoral condyles but also produced a metastasis in the inguinal lymph nodes.

Mangalik, V. S., and Lal Mehrotra, R. M.: Adamantinoma of the tibia; report of a case. Brit. J. Surg. 39:429-432, March, 1952.

Radiation Bone Tumors

Sensitive tissue including bone when subjected to ionizing radiation over a sufficiently long period and sufficiently excessive dosage may produce malignant changes. Osteogenic sarcoma of the long bones, jaw, spine, and pelvis occurred among radium and mesothorium dial painters during World War I. Similar effects have been seen among radium chemists and patients under radium therapy.

Edson, E. F.: Occupational radiation hazards. Brit. M. Bull. 7:57-63, Jan., 1950.

Reticulum-Cell Sarcoma of the Clavicle

A 16-year-old white girl entered the hospital because of a swelling in her right supraclavicular fossa of three months' duration. The mass continued to enlarge for the next ten weeks, with the development of numbness in the fingers of the right hand. The preoperative impression at this time was either cellulitis with abscess or neoplasm of the lymphoblastoma type. At exploration the mass was found to be surgically inaccessible and only biopsy was done. A diagnosis of highly malignant, reticulum-cell sarcoma was made and because of the extremely rapid growing nature of the tumor, it was believed to be relatively radiosensitive. Roentgen-ray therapy was administered through one supraclavicular port, measuring 10 by 15 cm., with 200 kv. at a target skin distance of 50 cm. At the present time the patient shows no evidence of recurrence of the tumor thirteen years following radiation treatment.

Lawrence, K. B., and Lenson, N.: Reticulum cell sarcoma; report of a thirteen-year survival following one thousand roentgens of x-ray therapy. J.A.M.A. 149:361-362, May 24, 1952.

Bone Tumors

The importance of alkaline-phosphatase activity in relation to tumors was stressed, since this activity can be quantitatively related to prostatic carcinoma and bone tumors and associated with changes in rate of growth. In discussing the effect of roentgen rays on normal bone, it was noted that there was no immediate measurable effect with less than 2000 r, there were detectable changes with doses of 2000 to 3000 r, and evidence of permanent damage with doses of 3000 to 4000 r was seen, with necrosis and disintegration occurring when more than 5000 r was given to adult bone. Radioactive elements have produced bone tumors in rats, rabbits, dogs, and mice, the formation and site of localization of the resultant tumors depending on the site of application of the radioelement and its distribution. While roentgenological diagnosis is the earliest method we have of diagnosing bone tumors, the clinical history of pain often precedes changes in the roentgenogram. Care should be taken in the study of the roentgenogram and repeated views taken if standard views are negative. Soft-tissue masses about destructive changes in the cortex or medulla, periosteal changes, sclerosis, and eburnation of bone should lead to the suspicion of bone tumors.

Phemister, D., Moderator: Panel on bone tumors. In *Proceedings of the First National Cancer Conference. [New York.] American Cancer Society, Inc. 1949; pp. 217-227.*

Primary Malignant Tumors of Bone

Louis Lichtenstein, M.D.

Before launching into specific details, it seems important to emphasize some basic general principles entailed in the recognition and appropriate treatment of bone lesions that may be neoplasms.

1. If a patient complains of persistent pain, swelling, or limitation of motion in an extremity or some other skeletal part, obtain good roentgenograms promptly. If these disclose a significant skeletal lesion that may be neoplastic, do not guess at its interpretation but obtain a reliable opinion. Roentgenograms are essential in determining the extent and topography of various skeletal lesions and in judging their probable behavior on the basis of what they have done to the bone. It must be recognized, however, that radiological interpretation has its inherent limitations and that, as a rule, biopsy is required for definitive diagnosis. Despite the impression that still prevails in some quarters, there are no pat formulas for the roentgen-ray diagnosis of bone tumors and most of the allegedly pathognomonic signs, while sometimes helpful, are often fallacious.

2. The problem in diagnosis should be analyzed before biopsy, since the choice of surgical procedure, whether curettement, resection, or amputation, varies with circumstances. Needle biopsy, incidentally, has only limited usefulness in the diagnosis of bone lesions. The planning of an advantageous approach often calls for good liaison between surgeon, radiologist, and pathologist. While this principle is generally recognized as sound, in actual practice many men pay only lip service to it and seek advice after the fat is already in the fire, so to speak.

3. Definitive treatment, whether by surgery or irradiation, should be predicated upon accurate pathological diagnosis. The time is long since past when it might be said with some justification that the clinical history, the roentgenogram, or the response to treatment was more valuable than the pathologist's opinion. The writer is unalterably opposed to blind irradiation of skeletal lesions held to represent tumors, except perhaps for palliation of obviously advanced malignant tumors in inaccessible sites. By the same token, he is categorically opposed to radical surgery undertaken on the strength of a roentgen-ray impression alone, however well-founded it may seem. What appears to be an osteogenic sarcoma, for example, justifying ablation of an extremity, may conceivably prove to be a lesion of metastatic carcinoma.

4. If roentgen-ray therapy is the treatment of choice, employ the smallest dose calculated to be effective. In general, a total tumor dose of 3000 r or more should be avoided because of the hazard of post-irradiation sarcoma (after a latent interval of five years or more).

5. In dealing with what appears to be a malignant bone tumor, before resorting to radical surgery, obtain expert opinion if there is any reasonable doubt in regard to the diagnosis of sarcoma. Apart from any medicolegal liability entailed, it is possible that the lesion is not so serious as you think. Thus, osteomyelitis may simulate Ewing's sarcoma on occasion, as may rapidly developing lesions of eosinophilic granuloma. Instances of aneurysmal bone cyst are not infrequently mistaken for aggressive giant-cell tumors and sometimes for osteogenic sarcoma. With reference to lesions held to represent osteogenic sarcoma, one must be particularly careful to make certain that the condition does not represent some other, less serious lesion exhibiting active new-bone formation for whatever reason, e.g., periosteal ossification, myositis ossificans (in an active stage), ossifying hematoma, and exuberant callus. In the matter of recognizing

From the Department of Pathology, Wadsworth General Hospital, Veterans Administration Center, Los Angeles, California.

and treating skeletal lesions in general, more mischief is done currently through overdiagnosis than through failure to recognize malignant tumors promptly.

6. If the malignant nature of a bone lesion has been clearly established, on the other hand, treat it without undue delay and as aggressively as may be necessary. The result of compromise and temporizing ("too little and too late") is usually complete therapeutic failure. In dealing with early chondrosarcoma, for example, delay may sometimes mean the difference between cure and ultimate fatality. This urgency may apply also to instances of central fibrosarcoma and primary reticulum-cell sarcoma, which can also be cured if they are appropriately treated before metastasis has developed.

Metastatic carcinoma is by far the most common malignant bone tumor and, as such, must weigh heavily in any consideration of differential diagnosis.

In this discussion, however, we are concerned with the primary malignant tumors of bone, which may be listed[1] as follows:

Chondrosarcoma (peripheral or central)
Osteogenic sarcoma
Fibrosarcoma
Aggressive or frankly malignant giant-cell tumors
Ewing's sarcoma
Tumors of hematopoietic origin—multiple myeloma; chronic myeloid leukemia; acute leukemias; malignant lymphoma (reticulum-cell sarcoma, "lymphosarcoma," and Hodgkin's disease)
Malignant hemangioendothelioma
Liposarcoma (?)
Chordoma
So-called adamantinoma of limb bones, especially the tibia

It is hardly possible in the limited space available to comment in any detail on the clinical and diagnostic aspects of each of the malignant bone tumors listed. It may be helpful, however, to highlight the salient features having a bearing particularly on treatment and prognosis of the major tumors at least.

FIGURE 1. Surgically extirpated peripheral chondrosarcoma protruding from the inner aspect of a rib. This neoplasm developed insidiously and was discovered by chance following a chest injury. The pleura was not yet invaded by tumor and the prospect for cure in this instance is good.

Chondrosarcoma

This may be either peripheral (arising through malignant change in the cartilage cap of an osteocartilaginous exostosis) or central (arising through malignant change in an enchondroma or developing independently). It is particularly in cases of hereditary multiple exostosis and of skeletal enchondromatosis (Ollier's disease) that one must be on the alert for early malignant change. Activated growth in a previously quiescent cartilage tumor should be regarded as presumptive evidence of malignant transformation. Chondrosarcoma ordinarily pursues a slower course than osteogenic sarcoma and metastasizes relatively late to the lungs, so that cure can be obtained in many instances by appropriate surgery—block excision in the case of peripheral chondrosarcoma and resection or amputation of the affected part for central chondrosarcoma (making certain of clearance by an adequate margin). If the initial surgical procedure is inadequate and the tumor gets one jump ahead of you, you may never catch up to it (Fig. 1).

Osteogenic Sarcoma

As compared with chondrosarcoma, osteogenic sarcoma is more frequent; it occurs, on the whole, at an earlier age

(with the exception of the occasional instances complicating Paget's disease), pursues a more rapid course, metastasizes to the lungs relatively early, and hence is more serious, even when amputation is resorted to as soon as the condition is recognized. The sclerosing tumors are readily identified roentgenographically (Fig. 2); the osteolytic ones require more skill in interpretation. Significant elevation of the serum–alkaline-phosphatase value is observed in most instances. The commonest sites of occurrence are the lower end of the femur, the upper end of the tibia, and the upper end of the humerus. Radiation therapy, even in high dosage, is ineffective. Prompt ablation or radical resection is the only procedure that offers any hope for cure, although the writer's experience leads him to believe that the five-year–survival rate is probably no higher than 10 per cent.

FIGURE 2. Sclerosing osteogenic sarcoma situated in the lower shaft of a femur (rather than the end of the bone).

FIGURE 3. Primary malignant neoplasm in the upper end of the humerus of an older woman, which proved on biopsy to represent a fibrosarcoma. Despite ablation, this patient developed pulmonary metastases within a few months.

Fibrosarcoma (Central or Medullary)

Like chondrosarcoma, fibrosarcoma of bone should be clearly differentiated from osteogenic sarcoma and regarded as an independent neoplasm. Such tumors accounted for 31 per cent of the five-year cures of so-called osteogenic sarcoma filed in the Registry of Bone Sarcoma (as of 1941). The roentgen-ray appearance of any particular fibrosarcoma is likely to be rather ambiguous (Fig. 3), although one may perhaps suspect the presence of a primary sarcoma from the moth-eaten or mottled rarefaction of the affected bone area (usually the end of a long bone). Some fibrosarcomas behave like aggres-

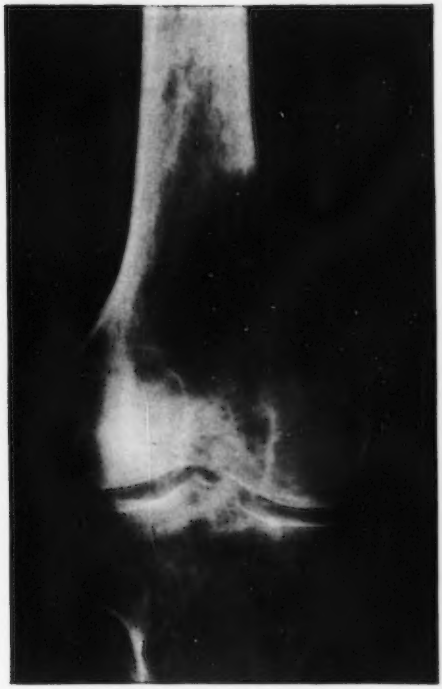


FIGURE 4. Aggressive giant-cell tumor, which recurred nine months after curettement. The neoplasm had broken through the cortex posteriorly and invaded the adventitia of the popliteal vessels, necessitating amputation.

sive neoplasms; others grow relatively slowly. In the latter instances particularly, cure may be obtained by radical surgery if the neoplasm has not already metastasized to the lungs. Any procedure short of amputation is likely to be unsuccessful.

Giant-Cell Tumor

Genuine giant-cell tumor (as seen in the lower femur, the upper tibia, or the lower end of the radius, for example) divorced of its spurious benign "variants" so-called, is a neoplasm not to be taken lightly. It is true that, given a sizable group of proved giant-cell tumors, approximately one half are likely to have a favorable outcome if properly treated by thorough curettement or roentgen-ray radiation. However, approximately one third are likely to prove more aggressive and recur after treatment (a considerable proportion of these may eventually come to amputation), and the remaining 15 per cent more or less will be frankly malignant and prone to metastasize to the lungs. An occasional giant-cell tumor will be found to be malignant on initial tissue examination, but more often one has to

FIGURE 5. Amputation specimen showing a Ewing's sarcoma developing in the lower shaft of a femur of a young woman who had complained of pain and some swelling for many months.

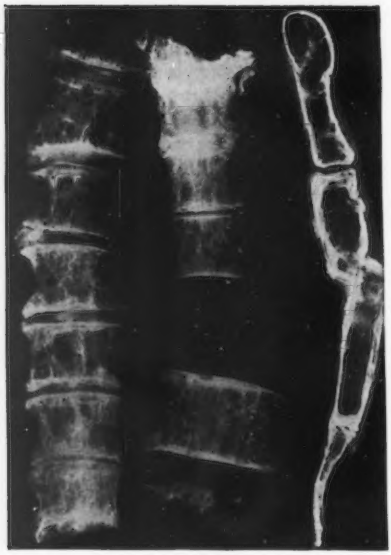


FIGURE 6. Skeletal changes observed at autopsy in a far-advanced case of mutiple myeloma, in the vertebral column and in the sternum, the body of which shows a previous pathological fracture.

reckon with malignant change incidental to one or more local recurrences. One must seriously consider the advisability of ablation as a life-saving measure for an aggressive giant-cell tumor that has broken through the cortex of the affected bone into the adjacent soft parts or that has recurred more than once despite well-conceived therapy (Fig. 4).

Ewing's Sarcoma

This neoplasm must be differentiated from metastatic neuroblastoma and carcinoma, as well as from multiple myeloma and malignant lymphoma. It is most commonly observed in the age group between 10 and 25 years. In most instances, only a single lesion can be demonstrated at the time the patient is first observed, although the tumor tends eventually to become disseminated throughout the skeleton and to metastasize to the lungs. The presenting lesion is commonly situated in one of the trunk bones or in a long limb bone. In the early stage of its evolution, such a lesion usually presents roentgenographically as a vaguely mottled area of rarefaction without any clearly discernible periosteal reaction, so that it may not be readily distinguishable from a focus of osteomyelitis. In a more advanced stage, when the tumor has already broken through the cortex and produced an overlying soft-tissue mass, its appearance will readily suggest a malignant neoplasm, although again this picture may not be at all distinctive and may at times simulate that of osteogenic sarcoma (Fig. 5). Roentgen-ray therapy achieves gratifying local amelioration but does not significantly inhibit spread of the neoplasm. Although there are occasional cures following radical surgery, Ewing's sarcoma carries a grave prognosis even under favorable auspices and the expectancy for survival beyond a few years is rather slim. Some of the more optimistic opinions expressed in the literature may well reflect the inclusion in the material analyzed of instances of primary reticulum-cell sarcoma of the bone marrow. The latter tumor, in contrast to Ewing's sarcoma, frequently responds well to appropriate therapy and has a 5- to 10-year–survival rate as high as 50 per cent.

Multiple Myeloma

This is a clinically and pathologically distinctive malignant neoplasm of the skeleton primarily, which seems clearly to originate from the hematic cells in the bone marrow and only occasionally in other extraskeletal sites. It is much more common than is generally suspected and undoubtedly many cases go unrecognized, more so in private practice than in hospitals. The condition has its greatest incidence in the age group between 40 and 60 years. Anatomically, practically every bone may ultimately come to be involved, more or less, in a given case. The progress of the disease may be steady and rapid, sometimes from the beginning and sometimes after a static period. In some cases, before the disease spreads over the skeleton, it may flourish in one bone (as a so-

called solitary myeloma) for months or even years. In an occasional case, myeloma cells may find their way into the blood stream in sufficiently large numbers to create a leukemic blood picture (so-called plasma-cell leukemia).

The roentgenogram is not necessarily that of multiple, lytic, punched-out defects in the calvarium and other bones (Fig. 6). One often observes merely some vaguely defined rarefactions, or generalized osteoporosis, or a single exuberant tumor, as noted. The lead to diagnosis may come from the discovery of anemia, the presence of myeloma cells in blood smears, hypercalcemia, hyperglobulinemia, evidences of renal damage of a peculiar type, and even the finding of unusual tumorlike amyloid deposits. None of the chemotherapeutic agents investigated to date has any demonstrated curative value. Problems in therapy are concerned mainly with palliation, particularly the relief of distressing bone pain and general supportive measures and also the handling of such complications as fractures of bones and compression of the spinal cord.

References

1. Lichtenstein, L.: Bone Tumors. St. Louis. C. V. Mosby Co. 1952.

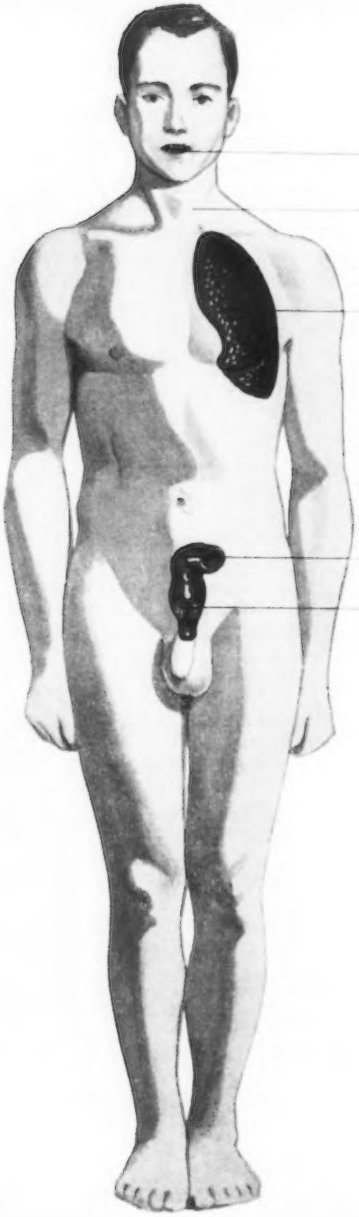
2. Macdonald, I., and Budd, J. W.: Osteogenic sarcoma. I. A modified nomenclature and a review of 118 five year cures. Surg., Gynec. & Obst. 77: 413-421, 1943.

Color Television

Date	Program Subject	Participants
Jan. 27	Cancer of the Larynx and Hypopharynx	Maurice Lenz, John D. Kernan, Arnold Bachman, and John N. Hanford.
	Cancer of the Thyroid	William B. Parsons and V. Kneeland Frantz.
Feb. 3	Cancer of the Skin	Thomas W. Stevenson, Arthur Purdy Stout, and Maurice Lenz.
	Cancer of the Central Nervous System	Lawrence Pool and Thomas Bridges.
Feb. 10	Lymphomas and Leukemias	Alfred Gellhorn, Edith Sproul, Ruth Guttman, and George Hyman.
Feb. 17	The Management of Advanced Cancer	Alfred Gellhorn, Ruth Guttman, Thomas Bridges, and Elliott Osserman.
Feb. 24	Cancer Detection	Cornelius P. Rhoads, Henry T. Randall, Emerson Day, George N. Papanicolaou, and Genevieve Bader.
March 3	Head and Neck Cancer	Hayes E. Martin and Attending Staff, Memorial Center.
March 10	Hormone Therapy in Inoperable and Recurrent Breast Cancer	Norman Treves, Henry T. Randall, Olaf H. Pearson, Joseph H. Farrow, and George C. Escher.
March 17	Cancer of the Lung	William L. Watson, George N. Papanicolaou, William G. Cahan, Alexander J. Conte, and John L. Pool.
March 24	The Significance of Indigestion	George T. Pack and Attending Staff, Memorial Center.
March 31	Advances in Control of Cancer of the Colon and Rectum	George E. Binkley, Michael R. Deddish, Lucille Loseke, and Maus W. Stearns, Jr.
April 7	Treatment of Recurrent Cancer of the Cervix	Alexander Brunschwig and Attending Staff, Memorial Center.
April 14	Cancer of the Genitourinary Tract	Willet F. Whitmore, Victor F. Marshall, and James L. Green.

Continued on page 27.

MALE

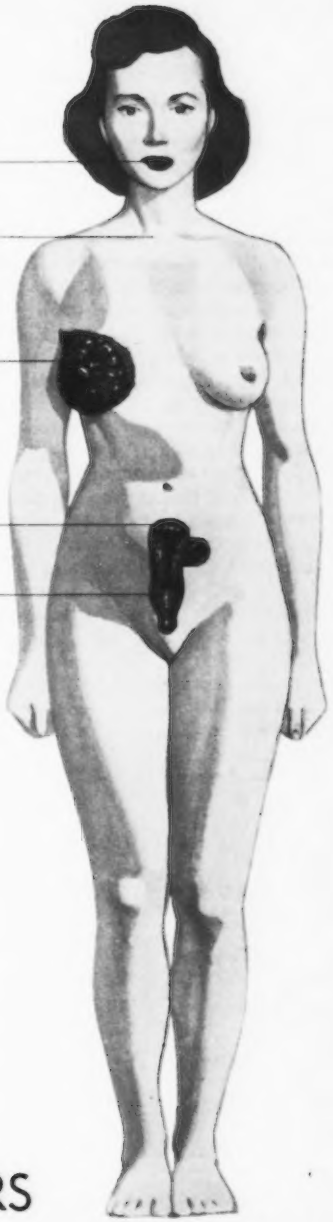


	%
MOUTH	6.3
SKIN	15.4
LUNG	9.5
RECTUM	6.5
PROSTATE	9.5
	47.2

INCIDENCE OF

FEMALE

	%
MOUTH	2.0
SKIN	10.7
BREAST	21.7
UTERUS	18.9
RECTUM	4.5
	57.8



SELECTED CANCERS

Benign Tumors of Bone and Soft Tissues

Ernest E. Aegerter, M.D.

The benign tumors of bone and related soft tissues constitute a heterogeneous group with behavior more characteristic of hamartoma than true neoplasm. Indeed, if one insists that growth of the true tumor must, by definition, be continuous and unrestricted, then all of these lesions, with the possible exception of benign giant-cell tumor of bone, probably fall into the hamartoma category. Their relatively innocuous behavior, however, does not lessen the exigency of accurate recognition, since overdiagnosis might conceivably result in the mutilating therapy that is necessary for the malignant lesions they may resemble both clinically and by roentgenogram.

Classification is difficult on a clinical basis because of the wide variety of anatomical sites and therefore a heterogeneous symptomatology. Though the exact cytogenesis of several of this group is unknown or unproved, they are all of mesenchymal origin and thus they can be classified according to the particular mesenchymal derivative from which they arise.

Each of the benign "tumors" of bone falls into one of three series, osteogenic, chondrogenic, or fibrogenic. There are no benign tumors arising from marrow constituents. The following is a list of the benign "tumors" of bone according to their mesenchymal derivation.

Osteogenic series
- Osteoma
- Osteochondroma
- Osteoid osteoma

Chondrogenic series
- Chondroma
  - Enchondroma
  - Ecchondroma
- Benign chondroblastoma

Fibrogenic series
- Ossifying fibroma (fibro-osteoma)
- Benign chondromyxoid fibroma
- Nonosteogenic fibroma (xanthofibroma)

Hemangioma of bone

Aneurysmal bone cyst

Giant-cell tumor of bone

It should be remembered that the stem cell of each of these lesions is a multipotential cell that the microscopist usually designates the "fibroblast." Actually it is no more a fibroblast than an osteoblast or a chondroblast and, depending upon its environmental condition, it may become any one of the three. Thus it should not surprise us to find that the microscopic appearance of these growths is confusingly similar and that mixtures of two or more lesion types are the rule rather than the exception.

The following is a brief description of each of the so-called benign tumors of bone:

The osteoma is an uncommon lesion that occurs in relation to the head bones, particularly those of intramembranous origin. It is usually discovered because of the symptoms it produces by growing into a paranasal sinus, the orbit, or from the hard palate. Its highest incidence is in young adults. It produces a rounded, encapsulated mass of bone tissue that is usually delineated by the roentgenogram. Its growth is slow and completely benign so that there is reason to feel that it is a hamartoma rather than a true tumor. It may represent the same process as the relatively more common hyperostoses of the calvarium, the latter going on to maturity and quiescence because they are symptomless.

The osteochondroma or osteocartilaginous exostosis is the most common "tumor" of bone. It usually manifests itself in the second decade, arising in the

From the Department of Pathology, Temple University School of Medicine, Philadelphia, Pennsylvania.

metaphyseal region of a long bone though it is occasionally seen affecting flat bones (pelvis and scapula). Since these tumors are active during the period of normal skeletal growth and cease to grow at the time of skeletal maturation, it may be argued that they are not true tumors but simply aberrations of bone growth. Essentially they are cylinders or pedicles of adult bone capped by an epiphyseal disk of cartilage. The lesion enlarges by regular enchondral ossification and ceases to grow by closure of the ossification center. It is usually symptomless but it may produce a bursa or interfere with tendon action. All of the periosteum of the pedicle should be removed if there is surgical intervention or if recurrence is possible. Reactivation after cessation of skeletal growth suggests change to a malignant neoplasm. About 5 per cent of these undergo such transition. The solitary osteochondroma cannot be differentiated from the lesion of multiple hereditary exostoses, though the hereditary factor appears to be lacking in the former.

The osteoid osteoma is a moderately common lesion occurring in the second and third decades in either the spongiosa or compacta of the long bones of the extremities or much less frequently in the small bones of the feet or the vertebrae. Usually its only symptom is pain, which may be quite severe, particularly at night. Point tenderness can often be elicited. The patient may not seek help for a period of months. The diagnosis is usually made by roentgen rays because of the highly characteristic roentgenogram consisting of an area of relative translucency usually not larger than a centimeter surrounded by an areola of sclerosis. Curettage is curative and the diagnosis is often confirmed by the relief of pain the moment the area is opened. There is no question now that it is a clinical and pathological entity, but there are grave doubts in the minds of many pathologists that it is a true neoplasm.

The two benign tumors of the chondrogenic series are the chondroma and benign chondroblastoma. The former usually occurs within the metaphysis of the bones of the hand, less commonly in those of the feet, and sometimes in the ends of the large long bones of the extremities. These are properly termed "enchondromas." Rarely they appear to arise from the outer surface of bone, presumably from the perichondrium, the most common site being the flat bones of the pelvis. These are sometimes called "ecchondromas."

Enchondromas have their highest incidence in the second and third decades, though it is not unusual to find them after the age of 30. They rarely cause pain until a minor injury results in fracture of the greatly thinned and weakened overlying cortex. A fusiform enlargement of the involved part may be the first sign. The lesions in the small bones of the extremities grow slowly, probably beginning in childhood, and, having reached a certain size, they become quiescent unless there is pathological fracture. They rarely undergo malignant change but I have seen one such case in a metatarsal bone. The enchondromas in the larger bones of the extremity are more apt to grow to massive size and eventually undergo malignant transformation.

The ecchondroma also grows slowly but a high percentage are either malignant from the outset or eventually become malignant. Myxomatous degeneration to some degree is almost constant in all cartilaginous tumors.

The benign chondroblastoma is a rare lesion that occurs in the epiphysis of the long bones of the extremities in the second decade. Since giant-cell tumor is the only other "neoplasm" that characteristically involves this area and since the latter rarely manifests itself in patients younger than 20 years of age, the diagnosis can often be made by roentgenogram alone. Pain is usually the only symptom and because of the area involved it is characteristically referred to the joint so that a monarticular arthritis must be ruled out. Despite the rather menacing appearance of the cells to the pathologist, complete cure is obtained by curettement.

The benign tumors of bone in the fibrogenic series include several rather uncommon clinical entities, the origin and

nature of which are obscure but the pathology of which is rather similar. Ossifying fibroma, benign chondromyxoid fibroma, and nonosteogenic fibroma are the lesions in point. All of these conditions have their highest incidence in the second and third decades and on a cytological basis they appear to be a variety of fibrous-tissue proliferation, one with bone metaplasia, one with cartilage metaplasia, and the last with a propensity for neither. All develop slowly, cause pain, and are completely cured by curetting. The sites of involvement and the roentgenograms are distinctive enough in each case, however, to consider them, at least for the present, as separate entities.

There are two types of ossifying fibroma, the commoner occurring in the jaws and a rare form somewhat more active cytologically found particularly in the vertebrae and sacrum. The latter is easily mistaken by the pathologist for osteosarcoma. The rare chondromyxoid fibroma is found in either flat or tubular bones and has been confused in the past with bone infarct. The nonosteogenic fibroma is the most common of the three types, occurring most frequently in the lower end of the femur. In large bones it has a tendency to be eccentric with a limiting border of calcifying osteoid that gives it a characteristic roentgenogram.

Hemangiomas may occur in bones just as they occur in skin, viscera, and other soft tissues; however, they rarely manifest themselves clinically. When they do, they are usually found in flat bones, particularly the vertebrae and skull. They may cause cortical expansion and pressure on nerve structures. Many produce a highly characteristic roentgenogram on which the diagnosis can be made. They may be found at any age but they are somewhat more common in younger patients. Roentgen-ray therapy has recently been advocated.

The aneurysmal bone cyst is a lesion most commonly found in the vertebrae but occasionally involving other flat and cylindrical bones. It causes pain and bone destruction, and the curious bleblike appearance of the overlying, thinned cortex is the most distinctive roentgen-ray feature. It is almost certainly not a true tumor and undergoes repair following surgery.

The giant-cell tumor of bone is an important lesion that deserves more than the exceedingly brief mention it gets here. Actually its incidence is considerably less than one might suppose if one relied solely upon roentgen-ray diagnostic reports. It develops insidiously causing bone pain and an inordinate amount of bone destruction. It always begins in the vicinity of the junction of an ossified epiphysis and the shaft and thus it is probably never seen in young patients in whom the epiphysis is still unossified. If these features are kept in mind most other lesions of bone can be ruled out on the roentgenogram alone. It should be remembered that a relatively small per cent of these lesions are true malignant tumors and only the experienced microscopist can differentiate them. The benign lesions will respond well to simple curettement.

The benign tumors of soft tissue are just as difficult to classify as those of bone. The following classification might be considered acceptable:

Fat (lipoma)
Muscle (granular-cell myoblastoma)
Fibrous tissue
- Nonspecific connective tissue (fibroma and desmoid)
- Periosteum, tendon sheath, fascia (benign synovioma, villonodular synovitis, giant-cell tumor of tendon, or extramedullary xanthofibroma)
- Supportive tissue of nerves (neurofibroma, neurilemoma)
- Supportive tissue of vessels (sclerosing hemangioma)
- Supportive tissue of skin (subepidermal nodular fibrosis)

For various reasons only a few of these need be discussed here. The granular-cell myoblastoma is a rather common lesion that occurs in relation to muscles and nerves. Almost half of them are found in the tongue. There is no agreement concerning the cytogenesis of this lesion. Some reports insist that there is a malig-

nant variety but most writers are agreed that it is completely benign and that, if a malignant behavior is manifested, it has been confused with a so-called alveolar soft-part tumor.

The true fibroma is a relatively rare lesion that arises from nonspecific fibrous tissue. It is of little clinical importance and, if most such diagnoses are examined critically, it will be found that they represent other more-specialized entities. The desmoid is a curious tumor-like lesion that deserves special attention. Most of them are found involving skeletal muscle or muscle sheaths. A number have been found arising from the outer layer of the periosteum, particularly of the pelvis of young women who have borne children. To the pathologist they present a picture of irregular aggregates of mature or nearly mature collagen-forming fibrocytes. They are locally invasive, however, and must be treated like malignant tumors. A rather common lesion arising from tendons or their sheaths, fascia, or apparently sometimes periosteum has been called the giant-cell tumor of tendons, villonodular synovitis, benign synovioma, or xanthofibroma. Most of them occur in relation to the flexor tendons of the fingers and palm, more frequently in women. A less common type is seen in relation to heavier tendons in the vicinity of a joint. These may begin as a proliferative response to inflammation or injury but they progress into a tumor-like nodule with a highly characteristic cytology. Rarely they may take on the attributes of an invasive desmoid with multiple recurrences.

This very brief discussion will serve to emphasize the complexity of this particular group of lesions. It should also emphasize that correct diagnosis is a matter of complete co-operation among clinician, roentgenologist, and pathologist. Anything less is apt to result in mistaken diagnoses and tragic overtreatment for lesions of more malignant behavior.

Color Television

The American Cancer Society Professional Education Color Television Series will pass the midway point in late February, 1954, as the series of fifteen programs from the Columbia University's College of Physicians and Surgeons, New York City, comes to a close. The television studio will then move to the Memorial Center for Cancer and Allied Diseases, which will be the originating point for the remaining fifteen weekly programs, which will extend through June 2d.

Audience reaction to the series has been excellent and there seems to be unanimous agreement that these "Cancer Conferences" are of great value to the medical profession. Many physicians have been obtaining informal study credit from the American Academy of General Practice through attendance at the telecasts. In several of the seven receiving sites the large attendance has called for reservation of seats.

The Memorial Center series will again emphasize the role of the general practitioner and what he can do to establish early diagnosis and promote a greater salvage rate of cancer.

Giant color-television projection screens (4½ × 6 ft.) have been set up for receiving the closed-circuit programs in seven cities—Boston, New York, Philadelphia, Pittsburgh, Toledo, Dearborn, and Detroit. Each program is color-kinescoped and the kinescope films will be available later to county medical societies, hospital staffs, and others through Divisions of the American Cancer Society.

A list of dates, subjects, and participants will be found on pages 17 and 27.

Sarcomas of the Soft Somatic Tissues

George T. Pack, M.D.

Sarcomas of the soft somatic tissues comprise one of the least frequent of all malignant neoplastic diseases representing less than 1 per cent of all malignant neoplasms treated at the Memorial Hospital. In a majority of instances the gross and microscopic pathological features of the tumor enable the clinician and pathologist to ascertain with some accuracy the histogenesis of the various types of sarcomas. In the order of their frequency are listed rhabdomyosarcoma, liposarcoma, malignant synovioma, Kaposi's hemorrhagic sarcoma, malignant neurilemoma, fibrosarcoma, dermatofibrosarcoma, and angiosarcoma. One group of these tumors defies classification even by selective staining, although identification by tissue culture might be possible if it were routinely applied; these sarcomas of undetermined histogenesis comprise the largest single series in our study. In this problem the surgeon is dependent on the tumor pathologist for the final label to be attached to each sarcoma; lest it be thought that this group of sarcomas of undetermined histogenesis contain the most anaplastic or undifferentiated and therefore the most malignant neoplasms giving a false outlook for curability of the specific histogenetic groups, it may be noted that the five-year definitive cure rate was 41.3 per cent, which is slightly better than the cure rate of 39.2 per cent that obtains for soft somatic sarcomas as a whole. Lymphosarcomas have not been included in this analysis.

Biopsy

If the tumor is ulcerating or fungating through the skin, a biopsy may be taken without hazard. For this purpose, I usually employ an endotherm loop with bipolar cutting current followed by electrocoagulation. If the neoplasm is small and noninvasive complete excision is the most feasible and safest step. The immediate or delayed report of the pathologist forms the basis for subsequent management, which would be a radical and therefore adequate dissection if it were malignant. Aspiration biopsy of these tumors is very helpful and is without danger in our experience. Experience in cytodiagnosis by the pathologist is necessary for the application of this procedure and too much must not be expected of it. It is enough if the minute tissue so removed can be classified as benign or malignant. Even this accuracy is occasionally impossible. The refinement of histological diagnosis usually must await fixed-tissue section study of the surgical specimen, but the surgeon can properly proceed if the diagnosis is "malignant tumor." A negative aspiration biopsy, which occurs in 15 per cent of our patients with soft-tissue sarcomas, never influences the subsequent management of the problem. A formal incisional biopsy of a sarcoma is attended by some dangers, such as hemorrhage difficult to control; spillage of soft, liquefying tumor; or/and ultimate fungation of the sarcoma through the wound. It is not always possible to suture the pseudocapsules of these sarcomas after an incisional biopsy. For this reason and particularly if the tumor be located in an extremity, the procedure should be done under tourniquet control, with frozen-section microscopic analysis and the institution of immediate radical surgical dissection or amputation.

Benign tumors of soft somatic tissues seldom become malignant; the majority of these sarcomas develop de novo, but there are occasional exceptions. Diffuse fibromas of fascia and tendon sheath on repeated recurrence may become invasive and ultimately metastasize. Malignant neurilemomas occur in about 10 per cent

From the Mixed Tumor Service, Memorial Center for Cancer and Allied Diseases, New York, New York.

of our patients with neurofibromatosis. Angiosarcomas have developed in these patients with congenital lymphangiomatosis. Bulky lipomas have undergone myxomatous, xanthomatous, and sarcomatous degeneration on rare occasions.

Regional Distribution of Sarcomas of Soft Somatic Tissues

Many fibrosarcomas and malignant neurilemomas are found on the extremities but their localization is not so specific as that of the other histogenetic types. Rhabdomyosarcomas occur preponderantly in the thighs and upper arms. Malignant synoviomas are found with surprising frequency on the hands and feet. Dermatofibrosarcoma protuberans has an affinity for the body trunk, anterior and posterior. Liposarcomas favor the shoulder and pelvic girdles for their development. Kaposi's idiopathic sarcoma usually begins on the feet with sporadic occurrences rarely in bizarre locations such as penis, tonsil, etc. In the retroperitoneum, liposarcomas, leiomyosarcomas, and malignant paragangliomas are found but with less frequency than lymphosarcoma.

Clinical Features

The malignant synoviomas may appear either as nodular or invasive, fixed, deep growths, often soft and pseudofluctuant. They are more tender than most sarcomas and sometimes cause considerable pain and disability. The synovioma tends to compromise adjacent bone either by infiltration or pressure atrophy. The fibrosarcoma may originate either as a lobular or diffuse neoplasm with a phenomenal tendency to recur after a seemingly adequate operation. On the extremities its course is that of upward or centripetal extension by direct growth until it actually infiltrates the pelvis or chest. Dermatofibrosarcoma protuberans is a skin tumor, originating in the corium and producing a multilobular agminated or cobblestone tumor of sometimes frightening aspect and relatively benign course. The epidermis is stretched tautly over the reddish-purple mass and may eventually rupture with fungation of the neoplasm. It may reach formidable local proportions before it infiltrates subjacent fascia and it seldom metastasizes. Rhabdomyosarcomas occur deep in the muscle bellies, may be multicentric in origin, are usually pseudoencapsulated, and rarely undergo liquefaction necrosis. Liposarcomas may be subcutaneous but more commonly are intermuscular and extend along the deep tissue planes. Soft-tissue radiography may show the tumor to be relatively translucent and contraction of the encompassing muscle groups gives the neoplasm a false ligneous consistency on palpation. Kaposi's sarcoma undergoes three phases in its evolution: first, a macular stage, in which the vessels are ectatic with lymphocytic infiltration; second, a nodular or granulomatous stage, in which there are proliferating vascular, granulomatous nodules in the skin and subcutaneous tissues; third, a neoplastic stage, in which the nodules become confluent and the component tissues of varied neoplastic elements, angiomatous, fibromatous, endotheliomatous, etc. This neoplasm may be of reticular-endothelial origin; we have reported its association with malignant lymphomas. The location and extent of retroperitoneal tumors may be determined not only by physical examination but also with the aid of excretory urography, gastrointestinal and colonic roentgen-ray studies, aortograms, and retroperitoneal pneumograms.

Surgical Treatment of Soft-Tissue Sarcomas

If the diagnosis has been established, the surgeon must judge as to extent of the sarcoma, its local operability, and the presence or absence of demonstrable metastases. If the tumor remains localized, the decision must be made as to whether a radical surgical dissection is possible of accomplishment or if amputation of an extremity is imperative. The pseudoencapsulation of some sarcomas offers a great temptation to the inexperienced surgeon to do a simple enucleation. Instead an ade-

Table 1

Malignant Tumors of the Soft Somatic Tissues

Comparison of Five-Year-Cure Rate of All Histological Types of Tumor

Histological type of tumor	Total cases	Determinate cases*	5-year cures No.	5-year cures %
Sarcoma of undetermined histogenesis	261	150	62	41.3
Rhabdomyosarcoma	105	65	22	33.8
Liposarcoma	100	64	23	35.9
Synovioma	60	37	8	21.6
Kaposi's sarcoma	48	28	8	28.6
Malignant neurilemoma	46	32	19	59.4
Fibrosarcoma	39	18	10	55.6
Dermatofibrosarcoma	39	13	9	69.2
Angiosarcoma	19	11	3	27.3
Total Cases	717	418	164	39.2

*Treated more than five years previously; available for end-result analysis.

quate dissection should be done with ruthless sacrifice of all muscle groups or fascial planes involved from the points of origin and insertion. It is a wise precaution to dissect the neoplasm so widely as never to encounter it during removal. Even important nerves and blood vessels are sacrificed without question whenever they are adherent to these sarcomas; blood-vessel grafts to replace segments of major arteries are now in common use. The dissection should be done with meticulous care and retraction should be done away from, rather than toward, the tumor. As an adjunct to local surgical removal, the possible value of radiation therapy must always be considered. I can cite numerous instances wherein technically inoperable sarcomas became resectable and curable after preoperative irradiation.

It is an erroneous opinion to believe that sarcomas of this type metastasize solely through the blood vascular system. The three varieties of malignant mesenchymal tumors that sometime metastasize to regional lymph nodes are malignant synovioma, spindle-cell sarcoma of undetermined histogenesis, and rhabdomyosarcoma. If the sarcoma is located closely adjacent to the group of lymph nodes into which it may metastasize, then the extent of the operation is so planned as to enable the surgeon to excise the primary neoplasm and the regional lymph nodes in one encompassing monobloc procedure, thereby removing the intervening lymphatics as well as the other condemned tissues. This procedure is not feasible whenever a long distance intervenes between the original sarcoma and the regional lymph nodes.

If a sarcoma of the soft parts metastasizes to the lungs as a spherical growth and a single metastatic focus is visualized even by tomographic scrutiny, it is proper to remove this tumor either by segmental resection or by lobectomy.

In the individual case, there is a constant battle of judgment between the wisdom of the more radical amputation and the need for preservation of an important part. So many factors interplay here, such as the regional involvement by the tumor, its encapsulation or infiltrative method of growth, that no set formula for management can be established.

End Results

The end results of treatment of sarcomas of the soft somatic tissues give some cause for optimism, with a definitive five-year–cure rate of 39.2 per cent for all patients treated more than five years ago (Table 1). The most dangerous of these tumors are the malignant synoviomas and the angiosarcomas.

Over and over again, through sensitiveness and delicacy, people will delay weeks, nay months and even years, before seeing a doctor, carrying their load of anxiety, and finding, perhaps, that when they do summon courage, or by force of circumstances are driven to consult a doctor, their malady is of too long standing to be efficiently cured.

Lord Dawson of Penn (1864-1945).

Odor Control for Wet-Colostomy and Ileostomy Patients

Virginia K. Pierce, M.D.

Several years ago we published an article in this journal on the care of the wet colostomy (CA 1:166-168, July, 1951). Since then we have had many letters from both doctors and patients requesting additional information and offering suggestions.

One of the most outstanding problems is the control of odors. There are two facets to this odor-control problem, viz., deodorizing of the appliance itself and the prophylactic neutralization of odors arising from body secretions and excreta as they collect in the appliances. Many products for deodorizing such equipment have been submitted and tested by our patients wearing a varied assortment of appliances.

The most satisfactory deodorant has been one submitted by Bee-Kem Products, available in three forms, all within a reasonable cost range.

A powerful concentrated liquid deodorizer, known as DO 8, is most efficacious in the care of rubber, plastic, metal, and glass equipment and has no harmful effect on them. This includes body appliances, household and/or hospital equipment, e.g., hot-water bottles, ice bags, rubber rings, rubber sheets, and plastic pillow cases and mattress covers. The washed appliances are allowed to soak for a given length of time to afford adequate freedom from odor.

The second important facet—the deodorizing of excreta as they collect in the appliances when in use—is accomplished by DEO-TABS. These are readily soluble tablets that may be inserted into any body appliance, whether it be plastic or rubber, in which secretions or excreta are accumulated. One, two, or more tablets are inserted into the bag or appliance each time after the bag is emptied, the number depending upon the amount and character of accumulation and the length of the period of holding. These tablets are available in large-sized economy bottles, but a small pocket container will solve the problem for the working day.

The manufacturers of these two products have also developed a combined detergent-deodorant, called DEO-KLEEN, formulated to give both cleansing and deodorizing action in one operation. This has proved efficacious in more than 80 per cent of the cases.

Some patients seem to present individual physiological problems that require further study.

If your local surgical supply house is not aware of these new products, write Bee-Kem Products, Inc., 342 Madison Avenue, New York 17, New York.

April 21	Tumors of Bone	Bradley L. Coley, Norman L. Higinbotham, and Robert E. Carroll.
April 28	Moles and Melanomas	George T. Pack.
May 5	Lymphoma and Leukemia	Lloyd F. Craver, Henry D. Diamond, Joseph H. Burchenal, David A. Karnofsky, Henry J. Koch, and Sophie Spitz.
May 12	Tumors of Childhood	Harold W. Dargeon and Attending Staff, Memorial Center.
May 19	Hormonal and Chemical Treatment of Cancer	Rulon W. Rawson, Joseph H. Burchenal, David Karnofsky, Olaf H. Pearson, and Joseph E. Rall.
May 26	Treatment of Patients with Advanced Cancer—Analgesia and Psychiatry	Raymond W. Houde, Arthur M. Sutherland, Charles E. Orbach, Morton Bard, and Ruth B. Dyk.
June 2	Frontiers of Research	Cornelius P. Rhoads.

Clinic on Bone Tumors

DR. JAFFE: For the sake of general orientation, it seems worth remarking that the tumors of bones make up a large and intriguing group of lesions. In the clinical investigation of them, the disciplines of surgery, pathology, and roentgenology converge and reinforce each other—perhaps more strikingly than in most other fields of medical practice.

In view of the variety of tumors that one encounters in connection with the bones, it seems advisable first to have in mind a very general orienting classification of them, such as is presented here. This allows for the easy pigeonholing of all the possible bone tumors into a few very general categories.

General Classification of Tumors of Bones

Tumors developing as primary lesions in bones
Tumors invading bones from overlying soft parts
Tumors metastatic to bones
Tumors developing at sites of pre-existing bone disease
Tumors developing at sites of damage to bone from noxious agents

In a clinic such as we are presenting here, it would obviously be impossible to discuss fully even the first of these categories—that is, the tumors developing as primary lesions in bones. We are limiting ourselves to the presentation of the clinical (including surgical), pathological, and roentgenographic problems raised by two cases: one of giant-cell tumor of the upper end of a tibia and one of chondrosarcoma of the lower end of a femur.

Case 1

DR. MILGRAM: The patient in the case of giant-cell tumor of the tibia was a woman of 58 who entered the hospital complaining of difficulty with the right knee, of six months' standing, but who had previously never suffered any major illness. The difficulty had started with sharp pain over the inner aspect of the knee. The patient limped for several weeks, but the trouble had subsided to dull aching and discomfort, apparently associated with slight temporary loss of

From the Hospital for Joint Diseases, New York, New York.

weight, by the time a roentgenogram was taken and the patient referred to us. Physical examination revealed slight atrophy of the thigh and increased local temperature over the front of the knee region but no restriction of motion of the knee on the affected side. Around the tibial tubercle there was a fluctuant, nonpulsating mass, about 1½ in. in diameter, over which the skin was not fixed. Tenderness extended from this area to the tibial margin of the knee joint, along the inner side. There were no masses in the groin, and the rest of the examination revealed no abnormality. Roentgenograms of the affected knee area were taken, and I would like to ask for comment on them.

DR. POMERANZ: As Fig. 1 shows, there is a large, osteolytic lesion in the proximal extremity of the tibia. On the inner aspect of the shaft, the cortex has been thinned, and, for some distance below the articular surface medially, the contour of the bone is bulged. Laterally, the lesional area extends into the external condyle of the tibia, leaving only a small area of it intact. Superiorly, the lesional area reaches to the articular surface in the region of the medial condyle.

In favor of a diagnosis of giant-cell tumor in this case is the age of the patient (more than 20), the precise location of the lesion in the affected bone (that is, in the end of the bone and the adjacent metaphysis), and the general roentgenographic appearance of the lesional area. However, one does sometimes encounter a lesion meeting all these criteria that may still not be a giant-cell tumor. For instance, if located in the area in question here, a fibrosarcoma of bone, a focus of metastatic cancer, or a focus of so-called plasmacytoma occasionally raises the question of differential diagnosis from giant-cell tumor. In any event, in connection with a lesion such as we have in this case, though there is strong presumptive evidence in favor of the diagnosis of giant-cell tumor of bone, it seems advisable that that diagnosis be supported by study of biopsy material and that definitive surgery be guided by the histological findings.

DR. JAFFE: I am certain that we will, in this case, be able to establish, at the time of the operative intervention, a definitive diagnosis from a small fragment of tissue removed from biopsy. In other words, I think it is perfectly safe in this case to proceed with any definitive surgical procedure contemplated, on the basis of the report from an open biopsy specimen subjected to frozen section.

One may ask, in this connection, whether a needle biopsy, made some days in advance of the contemplated intervention, might be preferable to the open biopsy at the time of the intervention. My answer to that would be "no." In the first place, while a needle biopsy might supply sufficient tissue to make the correct diagnosis possible, it would not furnish enough detail and context to satisfy me in regard to the histological detail of the lesion, whether it be a giant-cell tumor or not. In the second place, since we strongly suspect, on clinical and roentgenographic grounds, that the lesion is a giant-cell tumor, there does not seem to be much risk in doing an open biopsy, especially since the biopsy specimen would be taken under tourniquet protection.

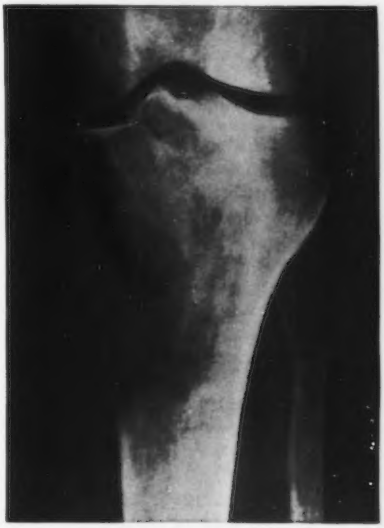


FIGURE 1

DR. MILGRAM: Tissue for the biopsy was removed from the fluctuant mass in the vicinity of the tibial tubercle, and the diagnosis of giant-cell tumor was confirmed by the pathologist. The definitive surgical procedure consisted of unroofing the upper 3 in. of the shaft of the tibia, removing all of the tumor tissue present, and implanting cortical and cancellous bone obtained from the posterior aspect of the patient's ilium. However, before the bone grafts were inserted, the wall of the cavity left after removal of the tumor tissue was cauterized with a 50 per cent zinc chloride solution. At the termination of the surgical procedure, the limb was immobilized in plaster.

In carrying out the surgical procedure in question, we were fully aware that, despite our effort to eradicate the lesion by local resection, a recurrence might, nevertheless, take place. Fortunately, in this case, a five and a half year follow-up showed that there was no recurrence, and the patient has been cured of her tumor and left with little or no functional disability. However, there are those who maintain that giant-cell tumor might well be treated with roentgen-ray therapy, without surgical intervention at all. I would like to ask for comment on this point.

DR. FRIEDMAN: In regard to irradiation I believe that a certain percentage of giant-cell tumors of bone can be arrested by this procedure alone. However, in principle, I advocate irradiation instead of surgery for giant-cell tumor only as a second choice. Specifically, I advocate it if the tumor is in a surgically inaccessible site or if it is so large that its removal would entail a serious mutilation of the part. However, giant-cell tumors in surgically inaccessible sites are rare in comparison to those occurring for instance at the ends of the predilected bones (femur, tibia, radius, and humerus).

There is another category of giant-cell tumor occurring in children and adolescents. These occur in the upper and lower jaws and in the flat bones. These lesions are radiosensitive and radiocurable. Their treatment should be primarily by irradiation.

DR. JAFFE: Irradiation therapy has the obvious advantage of avoiding surgical morbidity but it is the slowest form of therapy. Furthermore, it does not necessarily prevent severe deformity of the part. In regard to the cases seemingly cured by this method alone, we do not yet know so much about the likelihood of recurrence as we do for the cases treated surgically. We do know that radiotherapy may not forestall the occasional sarcomatous transformation of the lesion, and there is reason to suspect that it may sometimes even be a factor in eventually bringing this about. Finally, there can be little doubt that much of the enthusiasm for the treatment of giant-cell tumor by irradiation therapy (in preference to surgery) that one finds expressed in the older, and to a lesser degree in the current, medical literature is influenced by inclusion in the statistics of many cases in which the diagnosis of giant-cell tumor would not bear detailed scrutiny. In fact, those "giant-cell tumors of the jaw bones" to which Dr. Friedman refers are actually not giant-cell tumors at all. It is not surprising that they yield so readily to irradiation, for they are reparative granulomas of the jaw bones, containing sparse numbers of giant cells. They also heal readily when curetted.

Case 2

DR. MILGRAM: We proceed now to the case of the chondrosarcoma of the femur. The patient was a woman 37 years of age. Her disability, of three months' standing, had begun as a "heavy feeling" in the left thigh, just above the knee, and this feeling gradually changed to one of pain. Furthermore, a month before her first visit, the patient noted a tender spot above and to the outer side of her left kneecap. Neither the personal history nor the physical examination revealed anything significant, save for some fullness of the lower third of the left thigh, extending down about the knee, somewhat more marked laterally than medially. On palpation, the lower 6 in. of the shaft of the femur was found thickened and moderately but diffusely tender, especially medi-

ally and laterally. There was no increase of local heat, and no masses were palpable in the groin. All clinical laboratory findings were negative, except for a slightly elevated serum–alkaline-phosphatase value.

Roentgenograms taken in the course of clinical study of the patient revealed, in the left femur, a lesion that was suggestive of a cartilage tumor. In respect to the treatment of cartilaginous tumors, the interpretation of the biopsy specimen by the pathologist occupies a crucial position, for the borderline between benignancy and malignancy is often not sharp for these tumors. May I have some comment in this connection?

DR. JAFFE: To decide whether a given cartilage tumor is benign or malignant is often fairly easy, but occasionally quite difficult. The solitary central cartilaginous growths of long bones are often benign, but a fair proportion of them eventually undergo malignant transformation. The cartilage tissue of a benign growth may be but little calcified or heavily calcified. In any event, if one studies a biopsy specimen with the aim of deciding on the question of benignancy vs. malignancy, it will show in the benign lesion that, in fields in which viable cartilage cells are seen, the cartilage-cell nuclei are small. Cells with multiple nuclei are sparse.

The transition from benignancy to full malignancy in a cartilage growth is often a slow process. The evidence indicating early transition from benignancy to malignancy in the cartilage growth may have to be searched for in the tissue submitted for histological examination. Indeed, it can sometimes be overlooked, since it may be present in only a few microscopic fields. As such, the evolving malignant growth may be looked upon as representing an in situ chondrosarcoma formation.

There are, of course, also certain roentgenographic criteria for benignancy vs. malignancy in cartilaginous tumors, and some comment along these lines is now indicated.

DR. POMERANZ: The roentgenographic criteria of benignancy vs. malignancy in cartilage tumors of bone may be summarized as follows: Generally speaking, slow development, sharp delimitation, absence of periosteal stripping, and absence of involvement of the overlying soft tissues indicate that a given cartilage growth is benign. On the other hand, if the central lesion starts coming through the cortex and provoking cortical thickening and periosteal new-bone deposition, the growth is probably malignant.

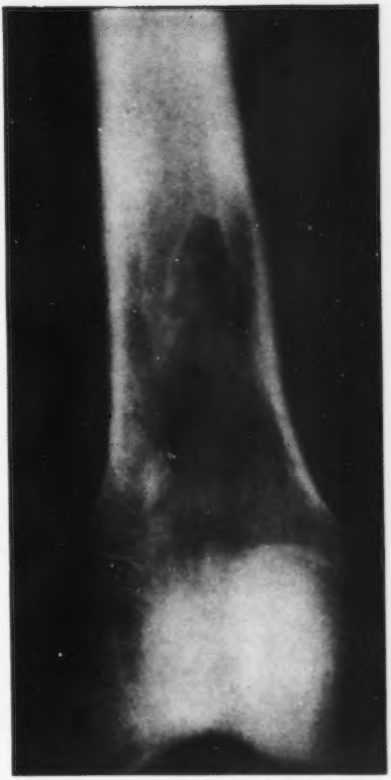


FIGURE 2

In the present case, the roentgenograms (Figs. 2, 3) revealed a fuzzy abnormal area in the lower portion of the affected femoral shaft. Anteriorly, the cortex seems to be thinned from the medullary side, and anterolaterally and medially there is a small amount of fuzzy, undulating new-bone deposition on the cortex.

FIGURE 3

It is difficult to decide, on the basis of the available roentgenograms, whether this cartilage tumor is benign or malignant.

DR. MILGRAM: To establish the diagnosis, a biopsy was done. The periosteum was found diffusely thickened, whitish, and irregular, and soft, gray-white, rather avascular tissue was found to have extended through the periosteum on the medial side of the femur, about 3 in. above the median epicondyle. Indeed, in this case, tissue removed at the biopsy posed no problem in regard to the diagnosis of chondrosarcoma. The pathologist reported that the cartilage tissue submitted showed considerable cellularity, large numbers of the cells had plump nuclei, many had double nuclei, and some few had bizarre nuclei. These findings indicated to him that the cartilage growth in question was a chondrosarcoma.

Since we had no way of knowing how far up into the femur the chondrosarcoma was extending, it was thought advisable to do a disarticulation at the hip joint, rather than an amputation through the femoral shaft. No difficulty was encountered in the healing of the incisions, but, after the disarticulation, the patient was troubled by "phantom limb" sensations. These were relieved by periodic injection (for nine days) of 2 per cent procaine into the sympathetic ganglia of L-2.

Despite encouragement, the patient could not manage crutches for four weeks, but by the sixth week she was walking well on one crutch and able to ascend and descend stairs. On her return home, an episode of depression occurred, interfering with her program of gait training. However, shrinkage of the stump continued and she consented, five months after operation, to being fitted with a prosthesis. Its use was a revelation to her, and with her resumption of social life she again took over the reins of her household. Seven months after disarticulation, she was quite free of her pain and was doing most of her housework for a family of three, with the help of a younger sister. She was last examined three years after the disarticulation operation. There was no evidence of recurrence locally in the stump or elsewhere. Her health continues normal.

Perhaps, before concluding, we should have some comment on the value of roentgen-ray therapy for the cartilage tumors.

DR. FRIEDMAN: From a practical clinical point of view, I must say that I have never arrested a chondrosarcoma with irradiation alone. Chondrosarcomas should be treated surgically, and irradiation be employed only for metastasis or when the primary tumor is so extensive or so unfavorably located as to be inoperable. In such cases, irradiation can sometimes achieve palliative prolongation of comfortable life.

DOCTORS DILEMMAS

Q *On a house visit to a couple who have recently moved to this city, the husband (a man of about 47 who was ostensibly* NOT *the patient) insisted on telling me the story of his illness three months ago. He had had "atypical pneumonia" and had two roentgenograms of his chest, one taken six weeks after the other, to show me. There was little or no interval change in the roentgenograms, which showed changes characteristic of the stated diagnosis. At the time the second roentgenogram was made, a bronchoscopic examination was reported negative. His wife informs me that the cough that he developed at the time the "atypical pneumonia" appeared still persists. I have urged him to come to the office for a "check-up" and for another chest roentgenogram, which he is reluctant to do.*

A Bronchoscopic examination will reveal the presence of cancer in only about 40 per cent of cases. Another roentgenogram of the chest should, of course, be obtained and a lateral view might be helpful. Cytological study of sputum or bronchial washings is suggested. Even if this and another bronchoscopic examination are negative, exploratory thoracotomy should be strongly urged unless the abnormal shadows in the chest have completely disappeared.

Q *A 74-year-old man has developed marked gastrointestinal complaints over a period of about six months. Recent roentgen-ray examination discloses multiple ulcerations in the stomach. A carefully regulated medical regimen has relieved most of his complaints after three weeks and I am hesitant to suggest surgery. What, if anything, further can be done to rule out gastric cancer?*

A Multiple gastric ulcerations are usually benign. Careful repeat gastrointestinal films should be obtained at intervals of one, three, and six months, and the patient's medical regimen should be continued. Unless additional symptoms appear, the possibility that these ulcerations were malignant is small. If further evidence of ulceration is noted, surgical exploration is, of course, mandatory. Cytological studies of gastric secretions might be considered if facilities are available for this work.

Q *I have recently seen a 53-year-old farmer who was treated successfully for a basal-cell carcinoma of the forehead three years ago. The treatment consisted of radiation therapy. The patient now has an atrophic, telangiectatic area secondary to the radiation at the site of treatment. I have two questions: Is it safe for this patient to expose the treated area to the rays of the sun? Is it likely that this man will develop additional skin cancers at other exposed sites?*

A The patient should certainly avoid unnecessary exposure to the sun and

should wear a brimmed or visored hat while out of doors. Atrophic skin is especially susceptible to injury with subsequent ulceration. He should be advised to wear long-sleeved shirts and should be told of the possibility that subsequent skin cancers may develop, which should have prompt attention.

Q *A young woman, aged 23, has been aware of a "lump" in the mid-line of her neck, anteriorly, for the past eight months. It measures about 0.4 cm. in diameter. She has just consulted me and is most anxious to avoid surgery. I feel it should be removed. The patient has no other obvious physical abnormalities and does not complain of any discomfort.*

A While this might be a thyroglossal-duct cyst, it most likely represents a benign thyroid adenoma. Your patient might be reminded that while approximately 90 per cent of thyroid nodules represent benign adenomas, the remaining 10 per cent prove to be carcinoma. Often the area of malignant change can be detected by microscopic examination only. It might be added that such single, solitary adenomas more frequently contain cancer than do multiple adenomas. Your patient should be urged to reconsider her decision and to have the tumor removed.

Q *I have a patient, a 40-year-old white woman, nullipara, who presents the following history. Two years ago she had an inflammation in the left breast that was treated effectively with penicillin and local therapy. Three months later a small (2 cm.), slightly tender, movable nodule in the same breast was brought to my attention by the patient. This one was removed and the pathologist's report was "benign cystic hyperplasia." Six months later a similar nodule was discovered in the right breast. This was removed and reported "benign." Now the patient presents herself with multiple small nodules in each breast with intermittent premenstrual tenderness. She has a normal cycle and has received no estrogen therapy. I should appreciate advice.*

A In view of the history it seems likely that this patient has a chronic mastopathy of a not unusual type. Because of the similarity of the present lesions to the two previously "benign" biopsy specimens, careful observation at regular intervals should suffice. In the event of any change in the signs or symptoms from the present pattern, surgical intervention should immediately be considered. Estrogens for any reason should be withheld during this period.

Carcinoma of the breast is reported more frequently in patients with a history of "chronic mastopathy" and for this reason the observation period should be quite critical. Many surgeons elect to do simple mastectomies for persistent "chronic mastopathy" after having exercised the usual precaution of frozen-section evaluation while the patient is on the operating table. With the postmenopausal atrophy, the symptoms of mastopathy commonly disappear so that its presence in such a patient warrants immediate biopsy.

WHEN Vesalius first practiced dissection of corpses, the Church was horrified. He was saved from persecution, for a time, by the Emperor Charles V, who was a valetudinarian, and believed that no other physician would keep him in health. But after the Emperor died, Vesalius was accused of cutting people up before they were dead. He was ordered, as a penance, to go on a pilgrimage to the Holy Land; he was shipwrecked, and died of exposure.

Russell, Bertrand: The Impact of Science on Society. New York. Simon and Schuster. 1953; p. 5.

new developments in cancer

Antiquity of Bone Tumors . . .

Ackerknecht (medical historian, University of Wisconsin) reports that tumors have been found in fossils of the cave bear, in fossil horses, in Peruvian Indians, in human remains in France and North America, and in Egyptian mummies as far back as 3400 B.C. He is of the opinion, however, that malignant tumors of the bone were more rare among prehistoric man and animals than today.

Radiation Sickness and Body Size . . .

Brown and Mahler (Postgraduate Hospital, London), from a statistical study of the latent period and the period of acute symptoms following single therapeutic doses of roentgen rays, conclude that the length of the latent period is dependent upon the dose and also upon the size of the patient. This indicates that a diffusible metabolite is the essential factor in development of symptoms occurring within a few hours of exposure to roentgen rays.

Plastics-Induced Tumors . . .

Oppenheimer (Columbia University) and Druckrey (Freiburg) have induced tumors, benign and malignant, in rodents by embedding cellophane and other plastics in the abdominal wall and in the peritoneal cavity. The tumors develop in one to two years. This may be significant in connection with the increasing use of plastics in human surgery, since, if it takes one to two years for a malignant tumor to develop in a rodent, it may take ten to fifteen years for a similar result in a human being.

"Lost" Drug Found . . .

Nine years ago, Cornman (then at Wistar Institute, Philadelphia) and others witnessed a biologist's dream come true—they added an early, crude penicillin to cultures of cancer tissue and saw the cancer quickly destroyed. Normal tissues growing in the same cultures were uninjured beyond a slight slowdown in their growth. When the investigators asked for more of the same strain of penicillin, they found that it was unavailable. New purification methods had been developed, and the commercial products lacked whatever cancericidal agent the crude penicillin contained.

Recently, however, Cornman (now at George Washington University) learned that some crude material had shown the same cancer-killing property. His investigation disclosed that the material was contained in two of twenty penicillin strains.

Broken down by counter-current distribution, five fractions of one strain re-enacted the miracle he had seen almost a decade ago. The factor, or factors, had been washed down the drain in purification. Schenley Laboratories have agreed to produce the material for Cornman's animal tests.

Antibiotics and Cancer . . .

Reilly and others (Memorial Hospital, New York) have tested more than 1200 crude antibiotic preparations against mouse sarcoma and found that only five caused sufficient inhibition to warrant further work. Of thirty-three known antibiotics none proved outstandingly tumor-inhibiting. Five—actidione, actinomycin, illudin M, illudin S, and terramycin—had slight tumor-retarding powers, but the last four were effective only at doses toxic to the host.

Radiation and Metastases . . .

Several investigators have studied the risk of cancer's spreading as a result of biopsy, but only a few have tested the potential of radiation in inducing metastases. Kaae (Radium Centre, Copenhagen) now has found that local irradiation (1 to 2000 r) of mouse breast cancer quadrupled normal lung metastases. Biopsy merely doubled the rate of lung metastases. Other investigators have found that radiation increased metastases to bone in rabbit sarcoma and distant metastases in another mouse mammary carcinoma—possibly because it facilitated entry of tumor cells into blood vessels.

Arginase and Cancer . . .

Unconfirmed claims of arginase as an effective drug against cancer still lack confirmation. Animal tests so far have shown arginase to be of no benefit. Greenberg and Sassenrath (University of California) found not only that the drug was ineffective against mouse cancers but that the biochemical reasoning that led to its use (that cancer patients exhibit a low content of arginase, which breaks down arginine, a growth-promoting amino acid reportedly abundant in cancerous tissues) is faulty. The California scientists found that there is no significant difference of arginase activities in the plasma, muscle, or liver of normal and tumor-bearing mice; that injected arginase temporarily reduced plasma-arginine levels but not those of the tumor; that administered arginase did not concentrate in the tumors; and that arginase, in several dosages, had no effect on tumor growth.

TEPA and How It Works . . .

TEPA, an ethylenimine, has caused regressions of some transplantable rat tumors and has been of some transient benefit to melanotic humans. How does it work? Crossley and others (Rutgers University) tagged the drug with radioactive phosphorus and traced it. They found a large concentration in the testes (whose growth it inhibited at high doses), a lower concentration in bone, a gradual accumulation in the spleen over a thirty-hour period (white-cell growth also was inhibited). In serum or plasma 60 per cent was associated with the globulin fraction and 20 per cent went to the nuclei or heavy components of liver, testicular, and tumor cells. About 65 per cent was excreted over a thirty-hour period.

The Ovaries and Breast Cancer . . .

The breast is one of the main target organs of estrogen. Oddly enough, while many investigators have examined the breast tissues of cancer-susceptible and cancer-resistant strains of mice, few have bothered to look at the ovaries. Fekete (Bar Harbor) now has noted qualitative and quantitative differences of ovaries in eight genetic mouse strains. She found that the ovaries of virgin mice susceptible to breast cancer (C3H) were very large, owing to the number and size of corpora lutea and the large number of follicles present. Resistant virgins (A and R III) had small ovaries and apparently produced proportionately little hormone.

St. Joseph's Hospital, Houston: Marcuse is studying the possibilities of determining malignant tissue by the length of time required for an excised specimen of tissue to start growing in culture. In many cases, malignant tissue starts growing within twenty-four hours, while benign tissue usually does not start growing for forty-eight hours or longer.

Tulane U.: Randolph has pitted a variety of physical forces simultaneously against each other in efforts to produce fine blood fractions -- natural gravity, centrifugation, buoyancy (centrifuge test tubes swing in a water environment), and electrophoresis. Krementz described transplanting embryonic guinea-pig thyroid and parathyroid tissue to a thyroidectomized human; apparently the implants did not take. Farber has found that androgens protect animals against ethionine-induced liver and pancreas damage, and estrogens enhance the damage; choline has cured rats' fatty livers; and methionine given with sucrose dissipated liver fat within hours. Segaloff has observed the virtual shutdown of the pituitary at certain periods in cancer patients; gonadotropic-hormone production particularly is depressed. Kurnick mentioned that DNase inhibitor has virtually knocked out the agent of lupus erythematosus in patients' serum. Kurnick and A. Carrera have decided, on the basis of their observations, that following removal of one kidney the remaining damaged kidney should be used as much as possible; if maximum function is not maintained, there may be progressive catabolism and irretrievable loss of function. Sternberg and others described a series of androgen-producing ovarian tumors and showed pictorially their virilizing effects and the dramatic return to normal with their removal. Heath showed how, after extensive animal tests, it was found that from two to eight wires could be implanted in the human brain and, under the stimulus of slight electric shocks, made to alter steroid-hormone patterns. The painless technique brought relief to some cancer patients suffering otherwise intractable pain. Ochsner recommended prompt surgery for frank and persistent gastric-cancer symptoms, radical surgery if cancer is found, and treatment of ulcers as cancer when they cannot be identified as either malignant or benign. Krementz and G. M.

Carrera have found microscopic examination of abnormal breast discharge helpful in diagnosis; they found one cancer and twenty-two intraductal papillomas by this means.

Louisiana State University: Burdette described his use of a "mutator gene," which apparently makes other genes mutate. It has produced all sorts of gynandromorphs in Burdette's extensive fruit-fly colony but apparently has not influenced tumor incidence. Burdette remains unconvinced that all cancers are a result of mutation. He points out that some carcinogens have not been shown to be mutagens.

COMING MEDICAL MEETINGS

Date 1954	Association	City	Place
Feb. 21-25	Latin American Congress of Otorhinolaryngology	Caracas, Venezuela	Centro Medico
Feb. 28-Mar. 4	Pan American Congress of Otorhinolaryngology and Bronchoesophagology	Mexico, D. F.	
Mar. 8-11	South Eastern Surgical Congress	Birmingham, Ala.	
Mar. 14-16	American Radium Society	Hot Springs, Va.	
April 8-9	American College of Physicians	Chicago	
April 9-12	American Association for Cancer Research	Atlantic City	
April 12-16	American Society for Experimental Pathology	Atlantic City	
April 24-30	Industrial Medical Association	Chicago	
April 26-May 2	International Congress of International College of Surgeons	São Paulo, Brazil	
May 3-5	American Association for Thoracic Surgery	Montreal	
May 3-5	American Society of Clinical Investigation	Atlantic City	
May 17-19	American College of Surgeons (Sectional)	London	
May 20-22	American Gynecological Society	Hot Springs, Va.	
May 31-June 3	American Urological Association	New York City	Waldorf-Astoria
June 2-5	American Proctologic Association	Los Angeles	
June 17-20	American College of Chest Physicians	San Francisco	
June 18-22	Canadian Medical Association	Vancouver, B. C.	
June 21-25	American Medical Association	San Francisco	
July 23-29	Sixth International Cancer Conference	São Paulo, Brazil	
Aug. 14-21	International Congress on Mental Health	Toronto, Ontario	University of Toronto
Sept. 7-10	International College of Surgeons	Chicago	
Sept. 12-14	New Hampshire Medical Society	Bretton Woods	
Sept. 12-14	Vermont Medical Society	Bretton Woods	

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